DOCTOR OF PHILOSOPHY

A Multi-methods Approach to Build Evidence-Based Practice for Using Silver Diamine Fluoride for Managing Carious Lesions in Children

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List of abbreviations

Silver Diamine Fluoride	SDF
Evidence-Based Practice	EBP
National Health Service	NHS
Systematic review	SR
Dental Professional	DP
Scottish Dental Practice Based Research Network	SDPBRN
Rapid Evaluation Practice	REP
Vocational Dental Practice	VDP
United States	US
Food and Drug Administration	FDA
Fluoride Varnish	FV
Toxic Substances Control Act	TSCA
Silver Modified Atraumatic Restorative Technique	SMART
Non-Restorative Cavity Control	NRCC
Glass Ionomer Cement	GIC
Atraumatic Restorative Treatment	ART
Matrix Metalloproteinases	MMP
Lethal Dose	LD
Environmental Protection Agency	EPA
United Kingdom	UK
Bio Medical Central	BMC
Corrected Covered Areas	CCA
Risk Of Bias In Systematic reviews	ROBIS

Latin American and Caribbean Health Sciences Literature database	LILACS
Biblioteca Brasileira de Odontologia	BBO
Number Needed to Treat	NNT
Weighted Mean Difference	WMD
Mean Difference	MD
Risk Ratio	RR
Prevented Fraction	PF
Randomised Controlled Trials	RCT
Grading of Recommendations, Assessment, Development and Evaluations	GRADE
Consolidated Criteria for Reporting Qualitative Research	COREQ
Hall Technique	HT
Statement of Dental Remunerations	SDR
Continuing Professional Development	CPD
General Anaesthesia	GA

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Finally, I wish to thank my wife, Elaf for putting up with me and our baby girl, Leah who arrived near the end of my PhD journey for being the best company in the lockdown, days (and nights!).

DECLARATION

I, Nassar Seifo, confirm that this is my own work, it has not been previously accepted for a higher degree and the use of all materials from other sources have been properly and fully acknowledged.

Nassar Seifo

Date 08/10 / 2020

Executive Summary

Introduction: In recent years, as a result of a better understanding of the pathology of dental caries, there has been a shift from traditional 'drill-and-fill' techniques towards more minimal-intervention, evidence-supported treatment options. Silver diamine fluoride (SDF) was first explored as a treatment option for managing carious lesions in Japan in 1969. SDF is a clear, odourless liquid containing silver and fluoride, which act synergistically to arrest carious lesions through a variety of mechanisms. It was cleared by the Food and Drug Administration in the United States in 2014 for managing dentine hypersensitivity. Since then, there has been growing global interest in its "off-label" use for managing carious lesions.

SDF became available for use in the United Kingdom in 2016, however, its use remains limited here. One reason for this may be that evidence alone does not provide clinicians with enough information to inform decisions, especially in relation to the adoption of new treatments or technologies. Ensuring that healthcare is not only underpinned by the best available evidence, but also includes the values and preferences of individual patients and clinicians, is the basis of Evidence-Based Practice. Although the three components make up EBP, research often focus on the best research evidence only and misses the latter two components.

Aim: To explore the use of SDF for managing carious lesions in children within the framework of the three components of Evidence-Based Practice; Best Research Evidence, Clinical Expertise and Patients' Values and Preferences.

Methods: This study comprised three arms, which directly align with the three components of Evidence-Based Practice:

(1) An umbrella review to explore the evidence for SDF's effectiveness for managing carious lesions. Five electronic databases were searched for Systematic Reviews investigating SDF for carious lesions prevention or arrest (1970-2018) without language restrictions. Systematic reviews were selected, data extracted, and risk of bias assessed using (Risk Of Bias In Systematic reviews) ROBIS tool, by two independent reviewers, in duplicate. Corrected covered area was calculated to quantify studies' overlap across systematic reviews.

(2) An exploration of Dental Professionals' views and acceptability of SDF. Semi-structured interviews with 14 dental professionals from National Health Service (NHS) Tayside and NHS Grampian were conducted. Interviews investigated dental professionals' existing knowledge and experience of SDF, if applicable, in addition to their perceived advantages, disadvantages, barriers and enablers to its use.

(3) An exploration of parents' and children's views and acceptability of SDF. A multi-method study with parents and children aged (4-12) years old was undertaken. The study comprised semi-structured interviews and a questionnaire-based survey to investigate parents' and children's acceptability of SDF treatment, including the barriers and enablers to its use, as well as their preferences.

Results:

Best Research Evidence

Eleven systematic reviews were included in the umbrella review; four focussing on SDF for root caries in adults and seven on coronal caries in children. These cited 30 studies (four root caries; 26 coronal caries) appearing 63 times. Five systematic reviews were judged to be "low", one "unclear" and five "high" risk of bias. Overlap of studies included across the systematic reviews was very high. SDF had a positive effect on prevention and arrest of coronal and root caries, consistently outperforming comparators. For root caries prevention, the prevented fraction was 25-71% higher for SDF compared to placebo (two systematic reviews with three studies) and prevented fraction 100-725% for root caries arrest (one systematic with two studies). For coronal caries prevention, prevented fraction = 70-78% (two systematic reviews with two studies) and prevented fraction = 55-96% for coronal caries arrest (one systematic review with two studies) with arrest rates of 65-91% (four systematic reviews with six studies). Eight systematic reviews reported adverse events, seven of which reported arrested lesions black staining.

Clinical Expertise

Thirteen of the 14 Dental Professionals interviewed were familiar with, or had some existing knowledge of, SDF. Four had used it to treat patients. Most Dental Professionals thought that the main advantage of SDF was that it required minimal patient cooperation. SDF was perceived as a simple, pain-free and non-invasive treatment approach that could help children acclimatise to the dental environment. However, the black staining of arrested carious lesions was reported as the main disadvantage and the greatest barrier to its use in practice.

Dental Professional participants believed that this discolouration may concern some parents fearing that the black appearance may instigate bullying at school or that others may judge parents as neglecting their child's oral health. They also thought that education of clinicians about SDF use and information sheets for parents would enhance the uptake of SDF in dental practice. Dental Professional participants believed that younger children might not be as bothered by the discolouration as older ones and anticipated greater acceptance of SDF for back primary teeth by both parents and children.

Patients' values and preferences

Parents' views did not differ from those of the Dental Professionals. Parent participants believed that SDF would be particularly useful for anxious or uncooperative children and the simplicity of the application procedure could make SDF an entry point to more complex procedures. They however expressed similar concerns to those of Dental Professionals that SDF-induced black staining could trigger bullying at schools or nurseries, if applied on front teeth, and suggested that this could subject them to judgment by others and accusations of being neglecting of their child's oral health. The children who were interviewed also expressed concerns about being picked on by their peers if they had discoloured front teeth. As a result, parents and children were more accepting of the SDF on non-visible back teeth. Parents' acceptance of SDF also increased if their child was less cooperative with the dentist or if SDF treatment avoided extractions under a general anaesthetic. In agreement with Dental Professionals' preconceived ideas, younger children appeared less concerned about the discolouration and the gender of the child did not seem to influence parents' decision-making nor the child's preferences regarding using SDF.

Conclusions: Despite the consistent supportive evidence reported in the systematic reviews included in the umbrella review for the use of SDF for arresting carious lesions in the primary dentition and Dental Professionals' awareness of it, uptake is still limited. Nevertheless, the potential advantages offered by SDF were acknowledged by both Dental Professionals and parents' who believed that SDF could be particularly advantageous for less cooperative and anxious children. Dental Professionals and parents agreed that SDF-induced black staining could be the main potential barrier to its use, with a concern raised that this could instigate bullying at schools or nurseries, especially for more self-conscious older children who showed a higher reluctance for receiving SDF on front teeth in their interviews. Dental Professionals suggested actions, such as developing SDF information leaflets or running courses to familiarize Dental Professionals with SDF that could help overcome some barriers they highlighted.

In conclusion, having explored the evidence available around using SDF, Dental Professionals' clinical expertise with SDF and patients' preferences regarding the child's dental treatment, SDF could be a valuable treatment regimen to manage dental caries in children.

Details of Publications

During my PhD study I had the opportunity to author and co-author several manuscripts. These publications can be found at the end of the thesis.

I firstly undertook training to conduct systematic reviews with the Cochrane Collaboration, Oxford. This allowed me to contribute to a Cochrane protocol for a systematic review concerning SDF for managing carious lesions:

- Rajendra, A., Oliveira, B. H., Ruff, R. R., Wong, M. C. M., Innes, N. P. T., Radford, J., **Seifo, N**., Niederman, R. & Veitz-Keenan, A. 2017. Topical silver diamine fluoride for managing dental caries in children and adults. *The Cochrane database of systematic reviews*, 2017.

I was invited to provide an academic commentary on a systematic review of SDF for the Evidence Based Dentistry Journal:

- **Seifo N**, Al-Yaseen W, Innes N. The efficacy of silver diamine fluoride in arresting caries in children. *Evid Based Dent*. 2018;19(2):42-43.

My skills were then polished enough to conduct my own review, so together with my supervisory team, I designed and conducted an umbrella review summarising the available systematic reviews concerned with SDF:

- **Seifo N**, Cassie H, Radford JR, Innes NPT. Silver diamine fluoride for managing carious lesions: an umbrella review. *BMC oral health*. 2019;19(1):145.

The logical next step was to publish an introduction to SDF to Dental Professionals by describing what SDF is, its mechanisms of action and presenting recommendations on how to use it and its indications and contraindications:

- **Seifo N**, Robertson M, MacLean J, Blain K, Grosse S, Milne R, et al. The use of silver diamine fluoride (SDF) in dental practice. *British Dental Journal*. 2020;228(2):75-81

After having undergone training on qualitative interviewing at The University of Oxford, my supervisory team and I designed a qualitative study to explore Dental Professionals' acceptability of SDF:

- **Seifo, N**., Cassie, H., Radford, J. *et al.* "It's really no more difficult than putting on fluoride varnish": a qualitative exploration of dental professionals' views of silver diamine fluoride for the management of carious lesions in children. *BMC Oral Health* **20,** 257 (2020).

Key Messages

KEY FINDINGS

- Although systematic reviews consistently supported SDF's effectiveness for arresting coronal caries in the primary dentition and arresting and preventing root caries in older adults for all comparators the limited number and questionable quality of the studies investigating SDF for preventing coronal carious lesions in children or managing carious lesions in the permanent dentition has to be taken into consideration.
- Dental professionals were aware that SDF can be used for arresting carious lesions. They had preconceived ideas that SDF-induced discolouration could be a barrier for many parents. Participants thought that education of clinicians and information sheets for parents would enhance the uptake of SDF.
- Parents believed that SDF would be useful for uncooperative children. Parents and children expressed concerns that SDF-induced black staining could trigger bullying, but they were more accepting of SDF on children's back teeth. Parents' acceptance of SDF also increased if their child was less cooperative with the dentist. Younger children appeared less concerned about the discolouration.

KEY IMPLICATIONS

- The findings of this study will contribute to the design of implementation strategies for the use of SDF in clinical practice by informing policy makers and decision making.
- The study has potential to encourage introducing SDF in the Statement of Dental Remunerations once it has been recommended by policy makers.
- The study suggests developing information leaflets about SDF containing the advantages, disadvantages, and expected outcomes to help introducing this treatment to wider population.
- The findings of this study advise courses to educate clinicians about SDF to familiarise them with its 'off-label' use.

FURTHER RESEARCH

- Exploring whether the socioeconomic status, educational level and residence location could have an impact on the level of parents' or children's acceptance of SDF.
- Conducting a qualitative study with children who have received SDF to gather their feedback and whether they had encountered any uncomfortable situations because of the SDF-induced black staining.
- Comparing the effectiveness of SDF and SDF followed by potassium iodide in arresting carious lesions in addition to parents' and children's acceptance of the SDF-induced black staining of each approach.
- Investigating the effectiveness of Silver Modified Atraumatic Restorative Technique (SMART) restorations or SMART Hall.

Thesis Structure

This thesis explores the use of Silver Diamine Fluoride (SDF) for managing carious lesions in children within the framework of the three components of Evidence-Base Practice: Best Research Evidence, Clinical Expertise and Patients' Values and Preferences. The introduction to each chapter orientates the reader and sets the context. The methodologies, results and discussions are distinct for each part of the project and are presented individually within each chapter. All findings are then brought together, and overall conclusions are drawn. The thesis comprises the following chapters:

Chapter One: An introduction to Evidence-Based Practice and how that applies to using SDF in practice.

Chapter Two: A literature review of SDF, exploring its uses, mechanism of action, adverse events, indications, contraindications and the application steps**.**

Chapter Three: An umbrella review (or overview of Systematic Reviews) concerned with SDF for managing carious lesions in children and adults to give a comprehensive assessment of what systematic reviews telling us about the effectiveness of SDF and include a synthesis of their results where possible**.**

Chapter Four: A qualitative study with Dental Professionals to explore their knowledge and experience of SDF and its acceptability, including the advantages, disadvantages, barriers and enablers to its use in practice.

Chapter Five: A multi-method study with parents and children to explore their views of SDF and what may influence their decision- making around its use.

Chapter Six: A final discussion bringing together all findings, followed by overall conclusions and recommendations**.**

CHAPTER ONE: BULDING EVIDENCE-BASED PRACTICE TOWARD USING SILVER DIAMINE FLUORIDE

1.1 Evidence-Based Practice

Evidence alone does not provide enough information for clinicians to be able to make decisions, especially if these might involve adopting new treatments, medicines or technologies (Bates et al., 2003). However, it can help support them and their patients in decision making as part of the care process. To ensure all healthcare is not only backed by firmly grounded evidence but still includes the values and preferences of individual patients and the clinical expertise available, the concept of Evidence-Based Practice (EBP) has been developed (Sackett et al., 1996).

Figure 1-1 Evidence Based Practice components

The most common definition of EBP is "*the conscientious, explicit and judicious use of current best evidence in making decisions about the care of the individual patient. It means integrating individual clinical expertise with the best available external clinical evidence from systematic research*" (Sackett et al., 1996). This means that EBP is the integration of clinical expertise, patient values, and the best research evidence into the decision-making process for patient care (Figure 1-1).

Clinical expertise refers to the clinician's cumulative experience, education and clinical skills (Wieten, 2018). The patient brings to the encounter their own personal preferences and unique concerns, expectations, and values. The best research evidence is usually found in clinically relevant research that has been conducted using sound methodology (Hughes, 2008).

Therefore, this thesis will consider the use of Silver Diamine Fluoride (SDF) in a clinical setting, within the framework of these three components of EBP.

1.1.1 Best research evidence

Evidence-Based Practice suggests that a hierarchy of evidence is needed to guide research and practice. The hierarchy of evidence was developed to enable different research methods to be ranked according to the validity of their findings and level of evidence (Evans, 2003). According to the Oxford Centre for Evidence-Based Medicine, well-designed systematic reviews (SRs) of randomised controlled trial are placed at the top of the hierarchical ranking (CEBM, 2009). SRs are increasingly being used for decision-making because they can give an overall all picture of the topic rather than looking at one piece of the jigsaw (Murthy et al., 2012). However, SRs themselves do not make recommendations, but inform guidelines that then adapt the findings of these SRs to make them relevant to the specific circumstances they are being applied to (Whitlock et al., 2008).

The number of published SRs has increased over time (Chalmers and Fox, 2016) and multiple SRs concerned with SDF have been published recently (Rosenblatt et al., 2009, Gao et al., 2016b, Chibinski et al., 2017, Oliveira et al., 2018, Oliveira et al., 2019). Reading all SRs can be confusing especially as there can be difficulty in identifying the one SR of the highest quality.

The Cochrane Collaboration (Cochrane, 2020) produces SRs often considered to be of the highest-quality, and these SRs usually contain reliable summaries of the evidence (Harvey, 2018) which are also presented in lay language. However, there are no published SRs including SDF as an intervention in the Cochrane

Library. A protocol for a SR entitled “Topical silver diamine fluoride for managing dental caries in children and adults” has been registered and was published in 2017, but the SR has not been completed yet (Rajendra et al., 2017) (**Publication *1***).

Therefore, a comprehensive Umbrella Review or overview of SRs concerned with SDF, to ascertain its effectiveness for the management of coronal or root carious lesions in children and adults, was conducted. Umbrella reviews are a relatively new methodology employed where multiple SRs address the same intervention and they aim to systematically bring together, appraise and synthesize the results of related SRs whilst identifying gaps in the area (Aromataris et al., 2015).

1.1.2 Clinical Expertise:

Clinical expertise means the judgment and proficiency that individual health care providers acquire through clinical practice and clinical experience (Wieten, 2018). Clinical expertise is vital to understanding and integrating the best research evidence into practice, to allow the formulation of recommendations to discuss with the patient. Without it, there is a risk of practices becoming tyrannised by external evidence, which cannot necessarily be applicable for all patients even if it was of excellent quality. Research evidence can never replace clinical expertise. However, informed by research evidence, clinical expertise decides whether this evidence applies to this individual patient and, if so, how it should be incorporated into a clinical decision. However, health care providers cannot be experts in every aspect and they need to be able to adapt evidence to fit with their own scope of practice (Sackett et al., 1996).

For the purpose of exploring Dental Professionals' (DPs) views' and clinical experience of SDF, a qualitative study with DPs was conducted. Semi-structured interviews, audio recorded with DPs, explored their views regarding treatment options to manage dental carious lesions in the primary dentition, with a focus on SDF.

1.1.3 Patients' Values and Preferences:

Patients are considered experts with a unique knowledge of their own health and their preferences for treatments and outcomes. Therefore, health care professionals are encouraged to involve them in treatment decisions and better patient involvement has been linked to improved quality of health outcomes (Say and Thomson, 2003). Patients' values and preferences are increasingly considered vital in healthcare policy decision-making. Many stakeholders explicitly support and appreciate patient's involvement and consideration of their preferences (Verkerk et al., 2006, Boivin et al., 2010).

It is generally acknowledged that health care providers' adherence to guidelines and the uptake of health intervention is determined by multiple factors (Fischer et al., 2016), such as the providers' personal beliefs and routines, in addition to factors determined by patient preferences such as patients' adherence to treatment and their satisfaction with treatment (Brazier et al., 2009). Acknowledging the value of the patient's perspective, a large body of research evidence on patients' preferences has become available, and new studies on patient preferences are increasingly being funded and embedded in empirical studies (Dirksen et al., 2013).

Integrating research evidence on patients' preferences in healthcare policy decisions is important for several reasons. Firstly, taking into account patients' preferences in healthcare policy decision may enhance the uptake of the healthcare interventions in its broadest sense. Secondly, integrating research evidence on patients' preferences may enhance consumer empowerment as patients' preferences and values can represent an important source of information. Thirdly, providing health care providers with results of research on collective patients' preferences may inform individual patient preferences in the context of health care decision-making. Finally, considering patients' views and values is ethically the right thing to do (Dirksen et al., 2013).

Since using SDF for arresting carious lesions in primary teeth is advocated to be the principal use of SDF, it was logical to explore both parents'/carers' and children perspectives and preferences for treatment options to manage dental carious lesions in children. Therefore, a multi-methods study involving semi-structured interviews and a questionnaire-based survey with parents/carers and children was conducted.

CHAPTER TWO: LITERATURE REVIEW OF SILVER DIAMINE FLUORIDE

2.1 Brief history

The antimicrobial properties of silver have been know and used for thousands of years, even before the germ theory was conceived (White, 2001). During his campaigns, Alexander the Great used silver urns for storing water for his armies. Later, pioneers trekking across the American West dropped silver coins in their containers of drinking water to halt the growth of algae and bacteria (Marx and Barillo, 2014). The Ancients Romans' first book of medicine describes how they used to place silver foils on wounds to facilitate healing. Even following the development of antibiotics silver continued to play an important role in medical uses and in the construction of medical devices such as parts of catheters, cardiac devices, sutures and other surgical appliances (Lansdown, 2006).

In the early 1800s, the use of silver nitrate ($AgNO_3$) was the first recorded use of silver in dentistry. Early American dentists used this extremely corrosive chemical to cauterise carious lesions to give an outcome similar to the dark hard crust observed on carious lesions that had arrested spontaneously (Stebbins, 1891). Silver nitrate gained increasing acceptance as a dental medicament. Indeed, G.V Black, the founding father of modern dentistry, described protocols for using it to arrest carious lesions in the early 1900s (Black, 1914).

This paved the way for another silver product, ammoniacal silver nitrate solution ($AgNH_3NO_3$), to be developed in 1917. This was advertised as an antimicrobial product that could penetrate into the dentine. This was known as "Howe's solution" and was used until the 1950s as a disinfectant in endodontic treatments to sterilise root canals following their preparation (Peng et al., 2012).

Later, in the 1970s, the Western Australian School Dental Service proposed a minimally invasive two-step approach to halt the progression of carious lesions in order to eliminate the burden of dental caries disease in this isolated area. Fluoride was advocated to be used in combination with silver to gain the dual advantages of both chemical elements. The first step was to apply silver fluoride (AgF), followed by stannous fluoride (SnF_2) to act as a reducing agent for AgF and to prevent of the development of new carious lesions. It was reported that this two-step technique led to the stabilisation of 74% of the approximal carious lesions and 90% of the occlusal surface enamel carious lesions; during a 24-month period, only 35% of all lesions required surgical intervention. For ethical reasons, no placebo group was included in the study and therefore, it was not possible to establish the relative efficacy of this treatment regimen (Craig et al., 1981).

In 1969, SDF was first investigated as part of Mizuho Nishino's PhD's thesis at Osaka University in Japan. She sought to combine the advantages of a high dose fluoride with the powerful antimicrobial properties of silver. This compound resulted in a chemical precipitate occluding the dentinal tubules and reduced dentine hypersensitivity (Nishino, 1969). Soon after, "diammine silver fluoride" was granted approval from the central pharmaceutical council of the Ministry of Health and Welfare of Japan as a cariostatic agent. The brand name for this agent was Saforide™ (Toyo Seiyaki Kasei Co. Ltd., Osaka, Japan), which has been marketed for over 40 years, and is still available today (Horst et al., 2016).

The correct terminology for $Ag(NH_3)_2F$ is diammine silver fluoride, although it is commonly misspelled or misnamed as "silver diamine fluoride". This is because it contains an "ammine" (NH_3) group, where at least one ammonia molecule NH_3 is bound with a metal ion (Figure 2-1) not an "amine", which refers to a covalently bound ($-NH_2$) group. However, the use of term diamine is now used so universal that it has become accepted in both marketing and within the scientific literature (Tsoi and Pun, 2020).

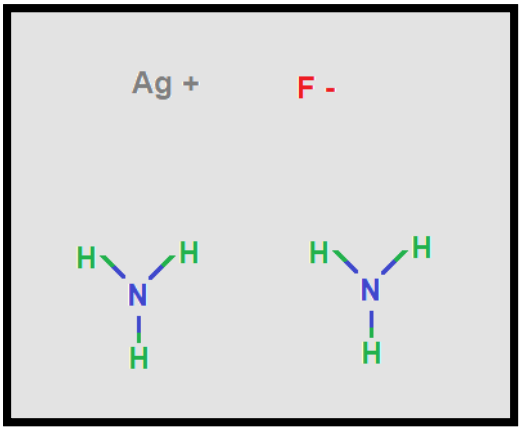

Figure 2-1 Chemical structure of SDF

Early studies investigating SDF resulted from a need for a novel agent to manage dental caries in developing countries, where there was limited access to oral health care.

SDF gained clearance from the United States (US) Food and Drug Administration (FDA) as a Class II Medical Device in August 2014 (Horst et al., 2016). Like 5% NaF Fluoride Varnish (FV), its approval for treating dentine hypersensitivity was granted on a "grandfathering" basis, because it had been in use before 1976, the year the United States Environmental Protection Agency passed The Toxic Substances Control Act (TSCA) law. This law regulated the introduction of new or already existing chemicals and when the TSCA was put into place, all existing chemicals were considered to be safe for use and subsequently grandfathered onto the list (Trasande, 2016).

SDF was classified as a medical device, rather than a drug because of its physical ability to block dentinal tubules, paving the way for expedited approval (Horst et al., 2016). In October 2016, SDF was awarded the designation of a 'breakthrough therapy' by the FDA (Horst, 2018), which identified SDF as a drug *"to treat a serious condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapy on a clinically significant endpoint(s)" (U.S. Food and Drug Administration, 2018).* This marked the first time that oral disease had been categorised as a serious medical condition and elevated its importance as an important public health issue (Sarvas, 2018).

2.2 The evidence for using SDF

SDF has been investigated for use in different areas of dentistry including disinfecting root canals during endodontic treatment, reducing dentine hypersensitivity, preventing and arresting carious lesions.

2.2.1 SDF for disinfecting root canals during endodontic treatment

SDF's antimicrobial action has made it a potential antimicrobial endodontic medication since successful endodontic treatment has been associated with the elimination of microorganisms in the root canals (Prada et al., 2019). Resistance of *Enterococcus faecalis* to different antibacterial agents used for disinfecting root canals has been reported (Law and Messer, 2004). The use therefore of 3.8% SDF has been proposed as an endodontic inter-visit medicament as it is presumed *E. faecalis* would not develop resistance. Saforide 3.8%, Toyo Seiyaku Kasei Co. Ltd (a 1:10 dilution of the 38% SDF solution) is a root canal disinfection agent and recommended to be used three times, at 24-hour intervals.

There have been several *in-vitro* studies investigating the effectiveness of SDF against *E. faecalis*. One study compared the effect of 3.8% SDF, 0.9% sodium chloride , saturated calcium hydroxide and 5.25% sodium hypochlorite against *E. faecalis* biofilms. Both SDF and sodium hypochlorite exhibited 100% reduction of *E. faecalis* after one-hour exposure time. In addition, silver deposits from SDF were observed on the radicular dentin surfaces, three days after application (Hiraishi et al., 2010). However, Al-Madi *et al* (2019) stated that sodium hypochlorite was more efficacious than 3.8% SDF against *E. faecalis* biofilm although the percentage difference in dead cells was marginal (62.26% for sodium hypochlorite and 57.39% for SDF). On the other hand, SDF showed significantly higher antimicrobial activity than 2% Chlorhexidine gluconate against *E. faecalis* biofilm (Al-Madi et al., 2019). This superiority of SDF, however, was not supported by Mathew *et el* (2012) who reported that 3.8% SDF and 2% Chlorhexidine gluconate showed similar anti-microbial activities. It has been argued that SDF could prevent reinfection of the root canal by inhibiting the formation of new biofilm.

SDF may cause root canal discolouration and therefore is not indicated for use in teeth in the aesthetic zone. Although the use of SDF as an endodontic medicament is plausible and has been shown to be effective in *in vitro* studies, robust clinical studies using clinical outcome are required to establish if it has a role clinically.

2.2.2 SDF for reducing dentine hypersensitivity

Dentine hypersensitivity is characterized by a sharp pain of short duration, arising from an exposed dentine surface and occurs in response to stimuli, typically

thermal, evaporative, tactile, osmotic or chemical and cannot be attributed to any other dental pathology (Holland et al., 1997).

It has been suggested that SDF can be used to treat dentine hypersensitivity because the aqueous silver and fluoride solution can produce a protective layer over the exposed dentine, partially plugging the dentinal tubules of the exposed dentine, thus reducing fluid shifts in the dentinal tubules (Mei et al., 2013a). However, even though SDF has been licenced for treating dentine hypersensitivity (Horst et al., 2016), there are a limited number of trials investigating its effectiveness. This may be attributed to the plethora of other management strategies and agents such as FV and dentine bonding agents (Scottish Dental Clinical Effectiveness Programme, 2013, Yadav et al., 2015).

There have been studies investigating the effectiveness of SDF for managing dentine hypersensitivity since the late of 1960s (Hatsuyama et al., 1967, Murnse and Takai, 1969, Kimura and Iso, 1971). More recently, SDF has been reported to be effective in relieving hypersensitivity to air (Castillo et al., 2011) and Craig (2012) suggested that SDF, followed by potassium iodide KI, reduced dentine permeability further after one week. This was attributed to the formation of silver iodide which had an additive effect when compared with the use of SDF alone. It was suggested that CO_2 laser can also further reduce dentine hypersensitivity when used after applications of SDF (Permata et al., 2018).

2.2.3 SDF for carious lesion arrest

With better understanding of caries pathology and evidence from clinical trials, dental caries is now considered a behaviourally-mediated, biofilm based disease rather than an infectious disease (Innes et al., 2019). Therefore, managing the

disease has shifted away from conventional strategies to cut it out and replace missing tooth without addressing the cause of the problem. The typical “drill and fill” approach requires complete carious tissue removal and restoration of missing tooth tissue. However, this surgical approach of managing carious lesions is no longer advocated and other approaches are becoming more acceptable (Innes et al., 2016a, Schwendicke et al., 2016).

Minimally invasive strategies such as, Stepwise Carious Tissue Removal, Selective Caries Removal (previously known as partial caries removal) and the Hall Technique have been shown to be equally as effective, or more successful, in managing the disease in the long-term, which suggests that the complete removal of carious lesions is not necessary to stop the progression of the disease (Innes et al., 2007, Schwendicke et al., 2016). However, it is not always desirable nor possible, to restore the remaining tooth tissue to its original form and a Non-Restorative Cavity Control (NRCC) option, therefore, may be an alternative for managing cavitated lesions. This does not involve removing carious tissue or placing a restorative material, but focusses on ensuring the cavity is accessible and that there is improvement in the patient’s oral hygiene by brushing and applying anti-cariogenic agents (van Strijp and van Loveren, 2018).

As part of a NRCC strategy, several silver compounds have been investigated. In the 1840s, silver nitrate was reported to be the first silver compound used for arresting carious lesions (Peng et al., 2012). Then in 1970, it was reported that the application of AgF followed by SnF_2 was effective in arresting carious lesions (Craig et al., 1981).

SDF was also introduced as a possible approach for managing carious lesions (Nishino, 1969). Since then, different SDF application protocols, including

different SDF concentrations and frequencies have been described (Seifo et al., 2019) (**Publication *2***). A single application of 38% SDF was reported to be effective in arresting carious lesions in primary dentition, although its effect appeared to decrease over time. In contrast, 12% SDF was not effective in arresting carious lesions (Yee et al., 2009). Similarly, when Fung *et al* (2016) compared the efficacy of annual and biannual applications of both SDF concentrations and found that the 38% concentration was more effective at arresting carious lesions in the primary dentition at 38% compared to the 12% concentration. In addition, biannual applications proved superior to annual application in arresting carious lesions and showed an arrest rate of 77% after 36-months in children (Llodra et al., 2005). In adults, an enhanced arrest rate of root surface carious lesions was observed when annual application of SDF was accompanied with biannual oral health education (Zhang et al., 2013). Compared to other interventions, annual application of a 38% SDF (Lo et al., 2001) or a 30% SDF (Duangthip et al., 2016) solution were reported to be more effective in arresting carious lesions in children than FV. Similarly, annual and bi-annual applications of SDF, proved superior in efficacy to annual application of high fluoride-releasing Glass Ionomer Cement (GIC) in arresting carious lesions. However, an improved SDF arrest rate for biannual application was shown compared to annual application (Zhi et al., 2012). 30% SDF also proved superior to Interim Restorative Treatment using GIC (a similar approach to Atraumatic Restorative Treatment (ART)) in arresting carious lesions in primary dentition (dos Santos Junior et al., 2012).

It has also been proposed that SDF can contribute to carious lesion arrest as a stage in restorative treatment; applying SDF as part of the ART approach (Frencken, 2014) is referred to as a silver modified ART (SMART) restoration

(Alvear Fa et al., 2016, Duffin et al., 2019), and when in combination with the Hall Technique, SMART Hall. Placing a restoration can be carried out immediately after the application of SDF or days or weeks later, after the carious lesions have arrested. The use of SDF followed by restoration placement may, by further potentiating carious lesion arrest, mitigate caries progression and reduce the chance of irreversible pulpitis. However, there are no randomised control trials investigating SMART's effectiveness compared to traditional ART or the Hall techniques.

It should also be emphasised that although there is evidence to support the use of SDF to arrest carious lesions, the consensus as to the optimum application protocol is still developing.

2.2.4 SDF for carious lesions prevention

In addition to the action of SDF to arrest carious lesions, it has been proposed that it has a role in preventing carious lesions because sound tooth surfaces showed strong resistance to carious lesions development when SDF was applied to arrest carious lesions (Chu et al., 2002b, Llodra et al., 2005).

There is some (limited) evidence that a fluoride releasing GIC can have a similar effect. However, this is limited to surfaces adjacent to the treated surface and of short duration (Liu et al., 2012). Similarly, it has been argued that in order to prevent caries, there has to be repeated SDF applications, although the efficacy for different protocols for application have not been established. Specifically, it has been reported that one application of 38% SDF's ability was inferior in preventing carious lesions on occlusal surfaces of permanent first molars in children, compared with ART sealants although ART sealants were more

costly and time-consuming to administer (Monse et al., 2012). However, annual applications of SDF have been found to be more efficacious in preventing carious lesions than both four times a year (Tan et al., 2010) in adults and twice a year application of NaF in children (Liu et al., 2012). Enhanced prevention in adults was reported when annual SDF application was accompanied with a biannual intensive oral health education (Zhang et al., 2013). Biannual applications of SDF over three years has been shown to have a greater percentage of efficacy in preventing carious lesions in primary teeth (80%) than in first permanent molars (65%) in children (Llodra et al., 2005).

In summary, there is evidence that frequent application of 38% SDF can prevent developing carious lesions although there is no standardised agreed protocol.

2.3 Mechanism of action of SDF

Despite SDF having been used for almost 50 years and investigated in diverse laboratory and clinical situations, the mechanism of action of SDF is still not been fully elucidated (Mei et al., 2013b). It has been proposed however, that SDF might operate through a variety of ways involving its two main ingredients, silver and fluoride (Mei et al., 2018).

2.3.1 Action of silver

2.3.1.1 Effect on cariogenic bacteria

SDF ionises in the presence of saliva and releases silver ions which have several antimicrobial effects (Figure 2-2) (Marx and Barillo, 2014). Firstly, silver ions can react can kill bacteria through the interaction of the bacteria cell wall which contains anionic and cationic charges. Silver ions can electrostatically bind to the

anionic charges of the wall. This leads to the inhibition of the movement of the cell or rupture or leak of the cell wall.

Secondly, silver ions can block the electron transport system in the cell and interact with life-sustaining enzymes. Silver ions are capable of inhibiting of the enzymes of the respiratory chain. They deactivate these enzymes through interaction with the thiol groups (-SH) on the enzyme's cystine molecules, causing the death of the organism (Russell and Hugo, 1994).

Thirdly, silver ions can interact with the guanine-cytosine and adenine-thymine within the organism's DNA present in the cytoplasm. This causes the mutation of the DNA and disabling the organism's ability to replicate which eventually leads to the death of the organism.

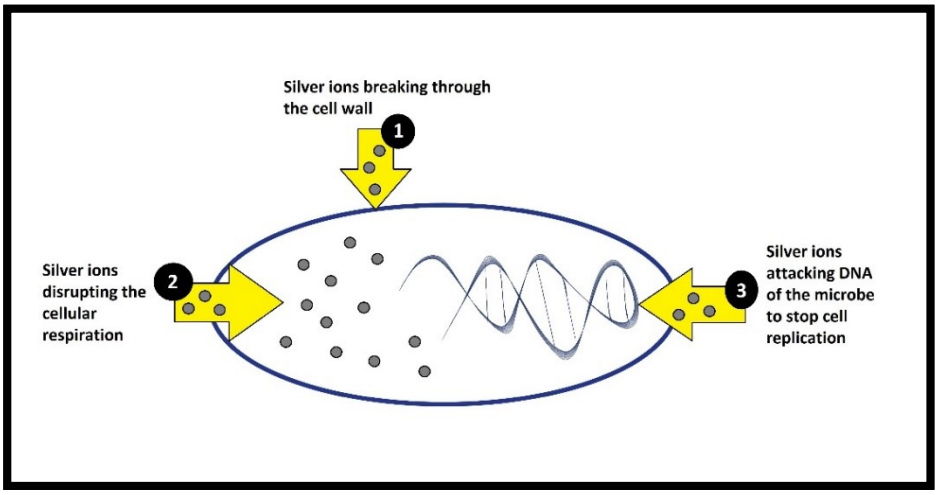

Figure 2-2 Silver ions action on cariogenic bacteria

A "zombie effect" has been described when silver in the dead bacteria is reactivated, killing live bacteria that are in intimate contact with the dead bacteria (Wakshlak et al., 2015).

2.3.1.2 Effect on tooth minerals

It has been suggested that the relatively insoluble, silver phosphate, formed by mixing enamel powder with SDF solution, can play a role in hardening of the arrested carious lesion (Suzuki, 1974). However, after immersing silver phosphate with artificial saliva, it disappeared and was replaced with silver thiocyanate and silver chloride.

Seto *et al* (2017) suggested that the carious lesion reaction with silver ions in SDF plays the major role in hardening the arrested lesions rather than the remineralisation mediated by fluoride ions. However, this assumption is questionable. If this was the mechanism, all silver-containing complexes could harden carious lesions. Mei *at al* observed silver nitrate-treated exposed dentine collagen was not hardened (Mei et al., 2013a, Mei et al., 2017). In addition, there is little information regarding the density of silver in the carious lesions to enable this putative mechanism (Buchalla et al., 2008). It is not clear to what depth silver can penetrate into the dentine. An *ex vivo* study did not find silver in the hardened region, whereas phosphate and calcium were observed in the outermost 150 μm of the hardened carious lesions (Figure 2-3) (Mei et al., 2014b). Moreover, silver chloride was reported to be the main precipitate since the solubility of silver oxide (1.3×10^{-3} g/100 mL) and silver phosphate (6.5×10^{-4} g/100 mL) is higher than that of silver chloride (8.9×10^{-5} g/100 ml) (Mei et al., 2013a, Mei et al., 2017). In summary therefore, silver ions are believed to have little effect on tooth minerals.

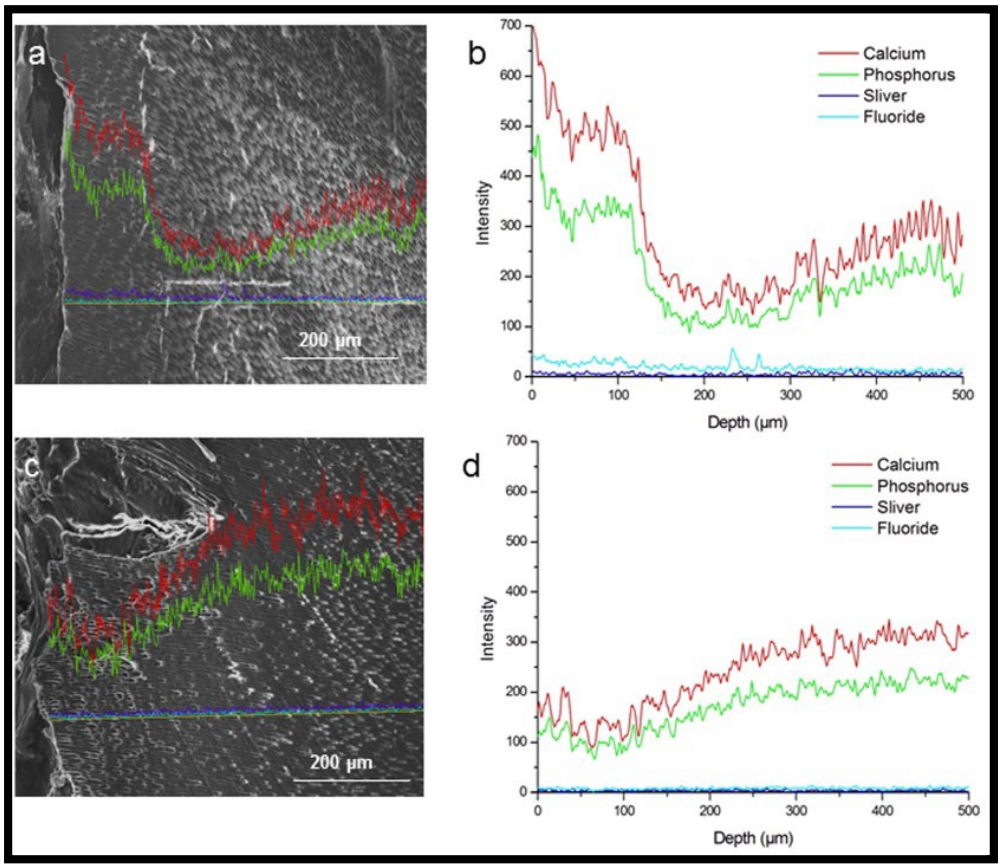

Figure 2-3 Elemental distribution of calcium, phosphorus, silver, and fluoride along the depth in the arrested carious lesion and active caries lesion. (A) Cross-sectional image of SDF arrested carious lesion. (C) Cross-sectional image of an active carious lesion. (B) Corresponding line-scan elemental profile of (A) along the depth of an arrested carious lesion. (D) Corresponding line-scan elemental profile of (C) along the depth of an active carious lesion. (Reproduced with the author's permission) Mei et al. (2014b)

2.3.1.3 Effect on dentine collagen

Following loss of tooth minerals and exposure of collagen to the oral environment, silver could inhibit caries-related dentine collagenase by interfering with molecules that break down collagen, such as matrix metalloproteinases (MMPs) (Chaussain-Miller et al., 2006) and cathepsin proteases (Tersariol et al., 2010). As shown in Figure 2-4, these contribute to dentine collagen degradation (Tjäderhane et al., 2013). When dental caries causes degradation of tooth minerals, the collagens get partially exposed to the oral environment and, therefore, degradation of extracellular matrix and denaturation of collagen starts, mediated by MMPs (Chaussain-Miller et al., 2006) and associated with cathepsin proteases.

This has been supported by the work of Mei *et al* (Mei et al., 2012, Mei et al., 2014a) that showed that 38% SDF inhibits the activities of MMPs and cathepsin proteases. It has been shown that silver has a moderate inhibitory effect on MMP-8 and MMP-9 and a stronger inhibitory effect on Cathepsin protease K and Cathepsin protease B.

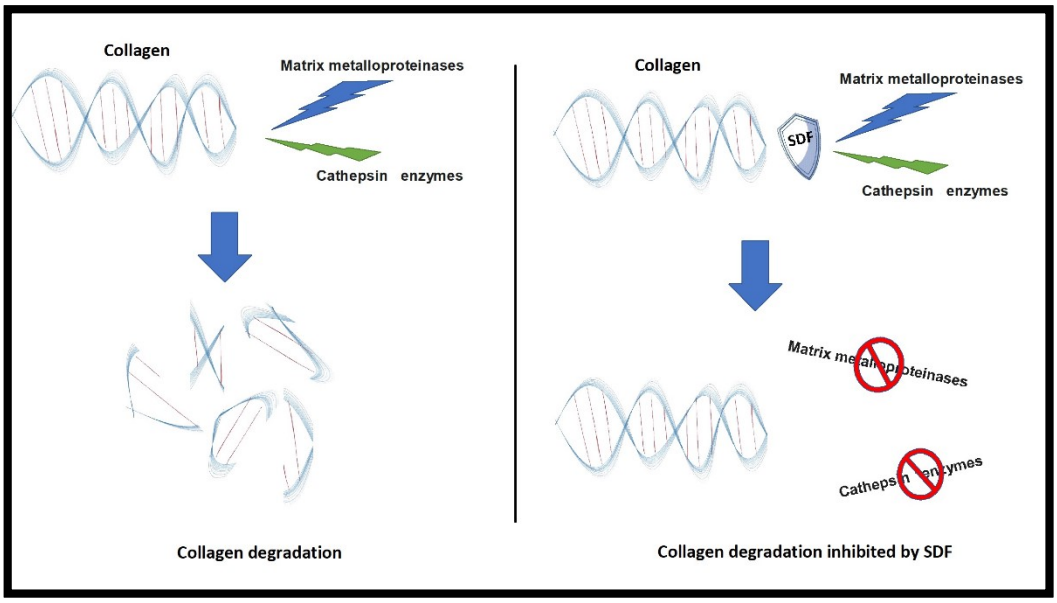

Figure 2-4 SDF's effect on collagen degredation

2.3.2 Action of fluoride

2.3.2.1 Effect on bacteria

Fluoride may inhibit plaque metabolism and acid production in the dental biofilm. Hydrogen fluoride can enhance the proton permeability of cell walls or inhibit the cellular enzymes (Koo, 2008). However, this effect is short-lived and may not play a significant role in caries reduction (Van Loveren, 1990). Therefore, chemical interactions between fluoride and hard dental tissues are considered the dominant mechanism in carious lesions arrest.

2.3.2.2 Effect on tooth minerals

It has been suggested that fluoride might react with hydroxyapatite crystals within the hard tooth structure. Different apatite crystals can be formed depending on the percentage of substituted fluoride ions. Fluorapatite ($Ca_{10}(PO_4)_6F_2$) is formed if fluoride ions completely substitute hydroxyl ions. However, complete substitution cannot be achieved in a clinical setting and in addition, Fluorapatite alone is not desirable as it is unstable (Chen et al., 2015). Where there is partial substitution of hydroxyl ions, a Fluorohydroxyapatite ($Ca_{10}(PO_4)_6(OH)_{2-2x}F_{2x}$, $0 < x < 1$) is formed (Figure 2-5).

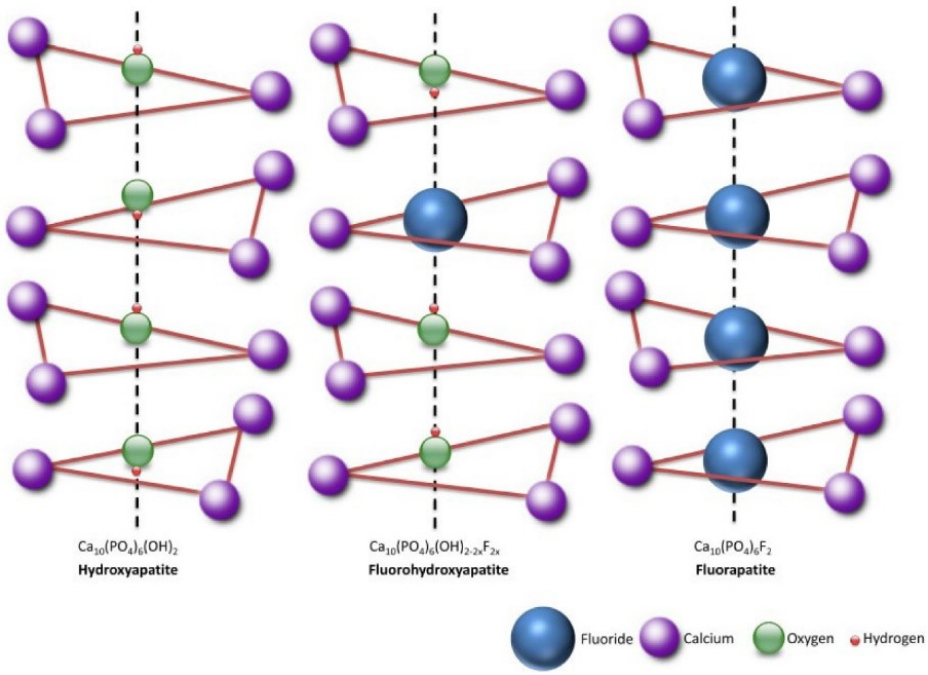

Figure 2-5 Crystal structure of hydroxyapatite, fluorohydroxyapatite, and fluorapatite (Reproduced with the author's permission) Mei et al. (2018)

HAp is chemically less stable than fluoride-substituted HAp (Okazaki et al., 1999). Therefore, the presence of fluoride-substituted HAp in the tooth structure can decrease tooth dissolution and, therefore, make it more resistance to developing carious lesions. Yet, it was difficult to detect fluorapatite (FAp) after SDF application because of the similarities of the crystal structures of FAp and HAp, or in some cases residual fluoride in the samples was below the detection limit such as that associated with energy-dispersive X-ray spectroscopy (Lou et al., 2011, Mei et al., 2013a). However, a more recent study used phosphate and calcium ions to simulate the salivary environment and showed that SDF application triggered fluoride ions exchange with hydroxyl ions and fluorohydroxyapatite (F-HAp) was formed after incubation (Mei et al., 2017).

It has been shown that a higher concentration of SDF leads to an increased fluoride content in the apatite (Mei et al., 2017). It is suggested that SDF can react with phosphate and calcium that leads to a mixture of FAp and F-HAp that firmly bind to the carious lesions, promoting remineralisation.

2.3.2.3 Effect on dentine collagen

Fluoride may contribute to the inhibition of dentine collagen degradation in two possible ways. Firstly, fluoride can inhibit proteinases activities. It has been reported that 150ppm of fluoride inhibited 79% of MMP-9 activity (Hannas et al., 2016). Similarly, 200ppm of fluoride was reported to inhibit MMP-2 and MMP-9 completely. However, the exact mechanism is unclear. It was suggested the high electronegativity of fluoride ions can inhibit the catalytic function of MMPs through binding with calcium and zinc ions (Kato et al., 2014). In addition, fluoride has shown inhibitory effects on Cathepsin proteases B and K (Mei et al., 2012).

Secondly, the apatite crystal formed from fluoride mediated remineralisation can protect collagen fibres. It has been reported, using exfoliated SDF-treated primary teeth, that the morphology of the surface of the arrested lesion was smooth with only few exposed dentine collagen fibres, in contrast to active carious lesions that was rough and porous, with exposed disorganised collagen fibres (Figure 2-6) (Mei et al., 2014b).

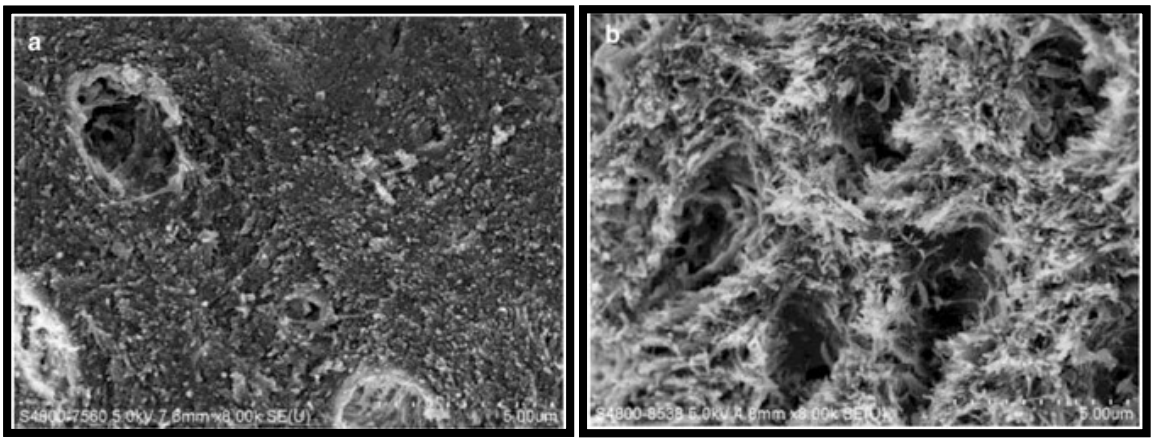

Figure 2-6 Surface morphology of arrested dentine caries lesion after SDF treatment (a) and active dentine caries lesion (b) under scanning electron microscopy. (Reproduced with author's permission) Mei et al. (2014b)

2.4 Maximum dose and safety margins

As part of the process of obtaining clearance by the FDA in the US, studies on rats and mice were conducted to determine the oral and subcutaneous lethal doses (LD_{50}) of SDF. LD_{50} is the amount of that chemical, given as a bolus which causes the mortality of 50% of tested groups of animals. The oral LD_{50} for SDF was 520 mg/kg, whereas the subcutaneous LD_{50} was 380 mg/kg (Horst et al., 2016).

One drop of SDF contains 9.5 mg SDF and this would be sufficient to treat five teeth. For a small child weighing 10 kg, this dose would be 0.95 mg/kg which is trivial in comparison to the LD_{50} (520 m/kg orally in rodents) (Horst et al., 2016).

Indeed, the actual dose of SDF is thought to be even smaller, as the largest dose measured when treating three teeth in each of six patients was 2.37mg (Vasquez et al., 2012).

The maximum recommended dose of SDF is one drop per 10 kg of the patient's weight per visit, allowing weekly intervals between visits. This is in line with the Environmental Protection Agency allowable short-term exposure of 1.142mg silver per litre of drinking water for one to ten days. The Environmental Protection Agency state that 1g of silver for lifetime exposure is safe and would not induce argyria where the skin turns blue or blue-grey (EPA, 1991). This would enable more than 400 SDF applications of the dose of 2.37 mg which, as previously mentioned, was reported to be the highest applied dose of SDF and was sufficient for treating three teeth (Vasquez et al., 2012). Weekly applications of SDF for three weeks annually was the most frequently used application regimen as described by Duangthip *et al* (2014).

SDF at 38% contains 44,800 ppm fluoride ions which is considered a high concentration of fluoride. However, one drop of SDF only contains 2.24 mg of fluoride (Crystal and Niederman, 2016) compared with a 0.5 mL dose of 5% FV which contains 11.3 mg fluoride (Hazelrigg et al., 2003). With biannual application dental fluorosis should not be a risk in children.

2.5 Adverse events

An adverse event is defined as *"adverse outcome that occurs while a patient is taking a drug or at some time afterwards but that may or may not be attributable to it"* (Aronson and Ferner, 2005).

No serious adverse events, such as allergic reactions, toxicity or pulpal irritations have been reported with the use of SDF (Seifo et al., 2019). However, if SDF inadvertently comes into contact with the gingiva or mucosa, a white mildly painful lesion can occur. Such heal within 24 hours after does not require intervention (Horst et al., 2016).

In a study examining the effectiveness of SDF to treat dentine hypersensitivity, no tissue ulceration, white changes, or argyria was observed in 126 adult subjects. However, a few experienced mild transient discomfort of the gingiva adjacent to the SDF-treated teeth (Castillo et al., 2011). In children, Duangthip *et al* (2018a) investigated adverse reactions when four different SDF application regimes were used. Minor adverse events, such as, oral pain, 'gum swelling', and 'gum bleaching' were observed only rarely and they argued were probably not related to the application of SDF These investigators concluded that SDF was safe to use in preschool children.

SDF cannot be used in people with an allergy to silver. The proposed incidence of contact dermatitis to silver containing compounds remains unknown, however this probably rare (Sterling, 2014). Desquamative gingivitis or mucositis can be relative contraindications for the use of SDF. However, placing a protective gingival barrier could mitigate the discomfort experienced by those with these mucosal conditions.

Therefore, SDF is reported to be safe in children with no allergy to silver. No serious adverse events associated with SDF have been reported and minor adverse events were rare.

2.6 Side effects

Side effects are secondary undesired effects that occurs when medication is administrated regardless of the dose due to the pharmacological properties (Aronson and Ferner, 2005).

SDF permanently stains carious lesions very dark and often black. However, non-carious or sound tooth does not become stained with SDF (Figure 2-7). This discolouration results from the oxidation of ionised silver into metallic silver.

A recent SR assessed parental acceptance of the discoloration cause by SDF and reported that the parental acceptance of SDF discoloration ranged from 29.7% to 95.4%. The parental acceptance was significantly higher in posterior teeth compared with anterior teeth, and for less cooperative children. Many parents accepted SDF treatment to avoid alternative treatment under GA. Parental perception of the discolouration was also Influenced by their socioeconomic status i.e. SDF was a favourable treatment for children with lower socioeconomic status because of its cost-effectiveness (Othman et al., 2019). Staining was reported to increase with higher SDF concentration and with higher frequencies of application (Duangthip et al., 2018a).

Several approaches have been suggested to mitigate the staining associated with the use of SDF. One approach is to use alternative compounds such as ammonium hexafluorosilicate and zinc fluoride. Whilst these may arrest carious lesions, they are not as effective as SDF.

It has been suggested that potassium iodide (KI) can react with excessive silver when applied immediately after SDF. Some SDF brands, such as Riva Star™ include capsules of KI along with SDF capsules.

The reaction product of silver iodide has been reported to reduce the staining *in vitro*. However, silver iodide is photosensitive and will eventually turn black when exposed to light.

Figure 2-7 Clinical photographs of carious lesions before and following application of SDF (Reproduced with athuors' permissions)

This use of KI to minimise staining associated with SDF is “off-label” since it is only approved to treat some chronic respiratory problems, and to protect the thyroid from radioactive iodine following radiation accidents. Potassium iodide is classified as a category D drug and therefore its use is contradicted in pregnant or lactating women unless its benefits outweigh the risks. The concern is that KI could overload the growing thyroid with iodide.

However, it is not clear whether KI does actually reduce discolouration of carious lesions when using it alongside SDF. A recent SR (Roberts et al., 2020) reported conflicting evidence and uncertainty for the effectiveness of SDF+KI in mitigating the long-term staining effect of SDF. Even though some studies reported a positive association between SDF+KI and minimal discolouration, other studies refuted these findings while others reported an increased blackening over time.

SDF can also stain the skin leaving a temporary henna-like discolouration (Figure 2-8). This, however, does no harm and resolves spontaneously within two weeks with the natural exfoliation of epithelial cells. However, longer-term staining could occur if submucosal or intra-oral wounds are exposure to SDF.

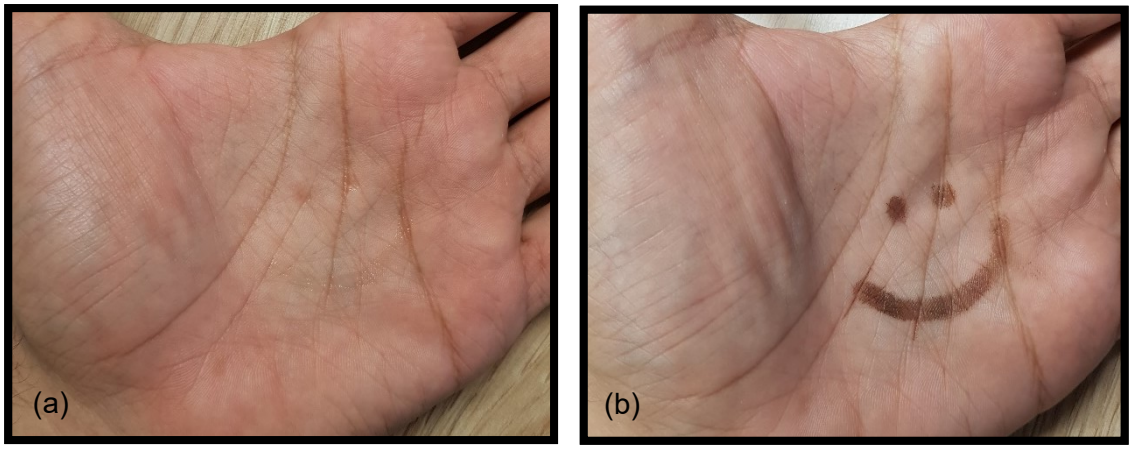

Figure 2-8 Skin after contact with SDF; (a) Immediately after contact, (b) 30 mins after contact

If SDF is spilled accidentally on clothes or clinic surfaces it could leave a black stain that is not easy to remove Figure 2-9. Therefore, immediate cleaning with water or a bleach containing cleaning products should be carried out if this occurs. Finally, patients may notice a bitter transient metallic taste during the application, but they can be reassured that this rapidly resolves (Horst et al., 2016).

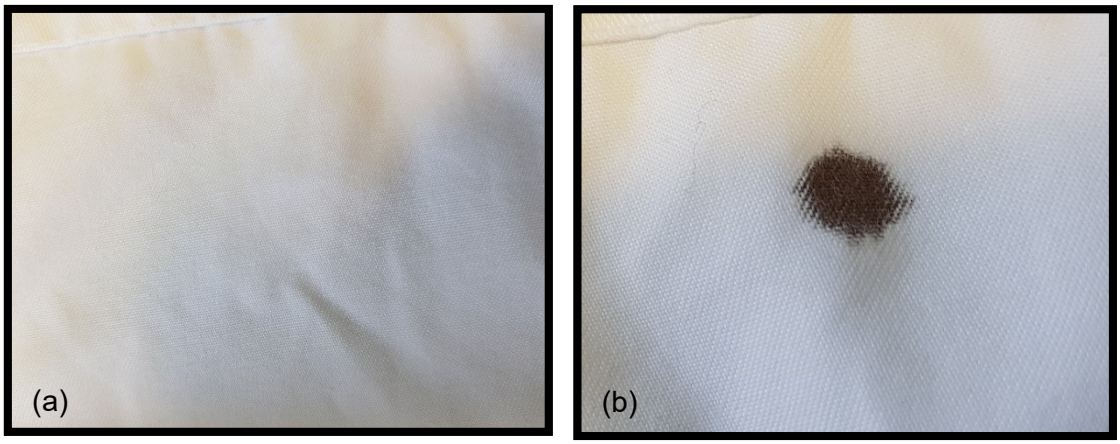

Figure 2-9 A scrub after the contact with SDF; (a) Immediately after contact, (b) 30 mins after contact

2.7 Clinical application of SDF

Several SDF applications regimes have been proposed (Horst et al., 2016, American Academy of Pediatric Dentistry, 2017, Seifo et al., 2020). However, all regimens agree on the effectiveness of repeated applications of SDF and stress on taking precautions to minimise any chance of inadvertent staining. Figure 2-10 presents the instructions for SDF uses proposed by Seifo *et al* (2020) (**Publication *3***).

Before use

1. Always handle with care, wear gloves and change them frequently during use to avoid accidental staining of hands or clinic surfaces.
2. Ensure dentist, nurse and patient have personal protective equipment on
3. Obtain informed consent from the patient and, where necessary from their parent/carer.
4. Take photographs at baseline and follow-up appointments to help record and assess the status of carious lesion if these are being treated. If this is not possible, there should be a written record of the status of the lesion.

Clinical application

1. Remove gross debris from cavitation to ensure SDF reaches the carious tooth tissue or area of the tooth it is being applied to.
2. Apply petroleum jelly to the lips to reduce the chance of temporary staining if inadvertent contact with SDF.
3. Isolate the area with cotton roll and apply gingival barrier if the lesion is close to the gingiva (the Riva Star kit has a barrier or use petroleum jelly). Alternatively, rubber dam can be used. However, take care not to coat parts of the carious lesion or tooth tissue it is being applied to.
4. Dry the carious lesion or tooth tissue with a gentle flow of compressed air or a cotton wool roll.
5. Pierce foil on silver capsule with a micro-brush.
6. Apply the SDF with a micro-brush directly onto the lesion or area of tooth being treated.*
7. Allow the SDF to absorb into the tooth via capillary action for at least 1 minute. Try to keep isolated for up to 3 minutes.
8. Blot excess solution to reduce the chance of it contacting the patient's tongue.**
9. 5% NaF varnish may be applied to the area if a carious lesion or MIH affected tooth is being treated as this may help to promote remineralisation.
10. Consider placing a dab of toothpaste on the patient's tongue if they notice a metallic taste

*If using KI, apply immediately after SDF application; pierce the foil on green capsule with a clean micro-brush and apply one to three times until no more white precipitate forms.

** If carrying out a silver modified ART restoration, encourage the patient to rinse after SDF application but before placing the glass ionomer

Follow-up

Follow-up at 2–4 weeks after the first application to check the activity of the carious lesion. Arrested carious lesions look darker and are hard to the touch i.e. when a ball ended probe is run across the surface. If the carious lesion is still active, a reapplication of SDF could be indicated.

Cavitated lesions can be restored after treatment with SDF. If they are not restored, bi-annual SDF reapplications show a better arrest rate versus one-time application.

Figure 2-10 Instructions for SDF use

2.8 The "Off-label" use of SDF for arresting carious lesions

The United Kingdom (UK) government services and information website (GOV.UK, 2014) states, the prescriber can use a medicine "off-label" when they are satisfied that an alternative, licensed medicine would not meet the patient's needs and the use of an off-label medicine would better serve the patient's needs based on the available evidence supporting its efficacy and safety.

The patient should be provided with sufficient information, at a standard relevant for that individual patient, about the proposed treatment, including potential adverse events, to enable them to make an informed decision. It may not be necessary to draw attention to the licence when seeking consent. However, it is good practice to provide as much information as patients or carers require or which they may see as relevant.

Riva Star™ SDF (SDI Ltd, Victoria, Australia) is licenced in the UK for treating dentine hypersensitivity (SDI Limited, 2016). The use of SDF to manage carious lesions is "off-label". However, there a body of evidence supporting its efficacy in managing carious lesions, and there is no alternative, licenced medicine that has been shown to be as effective. It is also used for this purpose in many other countries; in Canada and the US Advantage Arrest™ (Elevate Oral Care LLC, West Palm Beach, Florida, USA), a brand of 38% SDF, is approved for managing carious lesions. SDF was awarded FDA Breakthrough Therapy Designation for caries arrest in 2016 (Horst, 2018).

2.9 Indications and contraindications for the use of SDF

It has been suggested that SDF would be beneficial for numerous patients (Horst et al., 2016, American Academy of Pediatric Dentistry, 2017, Seifo et al., 2020):

- Pre-cooperative children who cannot tolerate other treatment approaches. This can be a final treatment for their primary dentition or a transient treatment while the child gets older and becomes cooperative enough to tolerate standard treatments. This “buying time” technique can help to avoid or delay treatment under sedation or general anaesthesia.
- Children or adults with medical or psychological conditions i.e. disabilities or dental phobias that would limit receiving standard restorative approaches.
- Patients at a high caries risk i.e. salivary dysfunction, Sjogren syndrome or other conditions.
- Patients with several carious lesions that cannot be treated in one visit and can become symptomatic while waiting the completion of treatment for all carious lesions. This might be particularly useful in dental schools’ settings where getting the complete treatment done could take a considerable period of time.
- People in deprived areas who do not have access to or cannot afford a “better” dental care would benefit from SDF treatments considering SDF is affordable and easy to apply.
- Finally, SDF would also be appropriate for cases where it is difficult to secure moisture control or isolation or where it might be difficult to gain the adequate access to the lesions for restorative success such as, root caries in furcation area, the occlusal of partially erupted third molar or caries at a crown margin.

SDF should not be used on lesions with clinical signs or symptoms of irreversible pulpitis, or dental abscess/fistula. Lesions with radiographic signs of pulpal involvement, or peri-radicular pathology are also contradicted for SDF treatments. Moreover, clinicians must be able to be flexible and consider other treatment approaches for lesions that do not become arrested with SDF applications over time.

SDF should not be used on patients with ulceration, mucositis or stomatitis. People with allergy to silver, fluoride or ammonia are also contradicted for SDF applications. KI should not be used in pregnant or breastfeeding women, patients undergoing thyroid gland therapy or on thyroid medication or patients with known allergies to potassium or iodine.

2.10 Summary

SDF was first introduced in 1969 in Japan to treat dentine hypersensitivity and manage by arresting carious lesions. The effectiveness of SDF in arresting carious lesions could be due to the synergistic effect of silver ions and fluoride ions in that silver ions inhibit biofilm growth, and fluoride enhances mineral deposition. Silver ions and fluoride ions also inhibit the activity of collagen enzymes and inhibit collagen degradation.

In contrast to some other countries, the use of SDF to manage carious lesions remains “off-label” in the UK, although this agent is licensed to treat managing dentine hypersensitivity. There is a body of evidence supporting its efficacy and no alternative, licensed medicine is available. In addition, it is used and approved for managing carious lesions in other countries.

No serious adverse effects such as allergic reactions, toxicity or pulpal irritations have been associated with SDF. However, SDF can cause permanent black staining of arrested carious lesions and also stains, skin, oral mucosa, clothes or clinic surfaces. If SDF comes into contact with the gingiva trivial irritation has been reported, that resolves spontaneously. A transient metallic taste may be noted. SDF cannot be used in people with an allergy to silver.

SDF may have a role in the care of pre-cooperative children, patients who have a high caries risk or poor access to dental care or those with medical or behavioural problems. It can also be used to treat any carious lesions at one visit.

CHAPTER THREE: AN UMBRELLA REVIEW OF SILVER DIAMINE FLUORIDE FOR MANAGING CARIOUS LESIONS: EFFECTIVENESS AND ADVERSE EVENTS

3.1 Introduction

This chapter of the thesis will focus on one of the three elements of EBP regarding the use of SDF for carious lesions management; best research evidence (Figure *3-1*) (Sackett et al., 1996*)*.

Figure 3-1 Best research evidence component of EBP

SRs aim to collect primary research data through identifying related research studies, appraising these studies and synthesising their findings into secondary research (Innes et al., 2016b). They usually offer the highest level of evidence, therefore, are essential in supporting health care decision making where it is required to inform clinical practice (Bero and Jadad, 1997). However, not all SRs are necessarily of good quality and reliable for decision making. The quality of SRs is directly related to the quality of the included studies and depends on the methodology followed and to what extent bias was excluded or minimised during the review process (Yuan and Hunt, 2009).

In addition, there has been a huge increase in the number of SRs conducted recently. It is estimated that around 8000 SRs of biomedical research are published every year (Page et al., 2016). Therefore, in areas where this is the case, the logical next step was to develop a new methodology to signpost decision and policy makers towards evidence that incorporates all of this evidence, synthesising it into one body and presenting its quality, as well as identifying any research gaps.

This rationale led to the development of umbrella reviews which also known in the scientific literature as overview of (systematic) reviews, (systematic) review of (systematic) reviews, summary of (systematic) reviews, or synthesis of (SRs) (Pieper et al., 2014b, Lunny et al., 2016).

Umbrella reviews aim to provide an overall picture of evidence regarding a specific topic and appraise related SRs not just repeat their findings; the role of the umbrella reviewer is to appraise the evidence from the SRs and not the primary studies. Umbrella reviews help to filter information by systematically synthesising information from related reviews of an intervention.

It is expected that the same study may be included in more than one SR investigating the same topic. Therefore, umbrella reviews should assess this and present a picture of the overlap in primary studies across SRs (Pieper et al., 2014a) to give the reader an estimate of the actual available evidence regarding the topic; more SRs does not necessarily mean more evidence. Moreover, this will enable the reader to assess the impact of the overlap on the umbrella review and allow them to interpret the results appropriately.

SRs have explored the effectiveness of SDF in prevention and arrest of carious lesions in children and adults (Rosenblatt et al., 2009, Gao et al., 2016a, Gao et al., 2016b, Oliveira et al., 2018, Oliveira et al., 2019). The ideal SR on which to base a clinical decision or guideline would be externally and internally valid, use a high-quality methodology, comprehensively include all evidence and carry out a meta-analysis (Jadad et al., 1998). Judging the quality of the evidence, interpreting the comprehensiveness of the evidence base and drawing conclusions about SDF's effectiveness to make clinical recommendations is complicated because a simple search in literature around SDF reveals numerous

SRs of different qualities and varied number of included studies. This can be attributable to discrepancies in inclusion criteria, different outcome measures and outcomes, variability in searches. However, this issue cannot be checked unless all relevant SRs brought together and assessed carefully. There is no single SR of SDF which is of obviously higher quality and recency than the others, and which should be prioritised in decision-making. By simply reading them it is difficult to interpret the implications of these discrepancies and have enough certainty over the entire evidence base to make a change to established clinical practice and predict the likelihood of treatment success.

The aim of this umbrella review was to give a low-bias, comprehensive assessment of what the evidence from SRs was telling us about using SDF for management of carious lesions in children and adults as well as the adverse events and side effects associated with SDF. It achieved this by collating the results of all available SRs of SDF and attempting to synthesise their results.

A concise version of this umbrella review has been published in the Bio Medical Central (BMC) Oral Health journal (**Publication 2**).

3.2 Objectives

To assess SRs, with or without meta-analyses, of the clinical effect of SDF for:

a) The breadth of evidence assessed in the SRs (SRs' characteristics and characteristics of their included studies);
b) The risk of bias of the SRs;
c) The effectiveness of SDF for arrest and prevention of root and coronal carious lesions in primary and permanent teeth;
d) Adverse events associated with SDF application.

3.3 Methodology

To ensure a high-quality approach and a transparent overview of SRs of SDF, the methodology proposed by the Joanna Briggs Institute for conducting umbrella reviews (Aromataris et al., 2015), Cochrane guidance (Becker and Oxman, 2011) and recommendations from a recent Cochrane symposium were followed (Pollock et al., 2016). The protocol for this umbrella review was registered with the prospective register of SRs (PROSPERO) (CRD42017070063) (Seifo et al., 2017) **Appendix** *1*

3.3.1 Inclusion criteria

3.3.1.1 Type of review

SRs with/without meta-analysis that included a thorough plan and search strategy and aimed to minimise bias by including and synthesizing all relevant studies.

3.3.1.2 Participants

Children and adults with or without carious lesions in primary and/or permanent teeth, on the crown and/or on the root surface.

3.3.1.3 Intervention

Topical application of SDF of any concentration or frequency, with or without caries excavation, compared to active comparators, placebo or no treatment.

3.3.1.4 Outcomes

Primary outcome: Carious lesions prevention or arrest using any outcome measure.

Secondary outcome: Any reported adverse events associated with SDF application.

3.3.2 Exclusion criteria

Primary studies investigating SDF or reviews that did not meet the definition of SRs; included a thorough plan and search strategy and aimed to minimise bias by including and synthesizing all relevant studies (Uman, 2011).

3.3.3 Databases and search strategy

PubMed, Embase, Cochrane Database of SRs, Joanna Briggs Institute Database of SRs and Implementation Reports, and PROSPERO were searched between 1970 and June 2018 (this time period was chosen because the first study investigated SDF for managing carious lesions was conducted in 1969).

Searches were built around the key words: "silver diamine fluoride" OR "silver diammine fluoride" OR "diamine silver fluoride" OR "diammine silver fluoride" OR "silver fluoride" AND "caries" OR "carious" OR "decayed" OR "cavity", AND "review" OR "meta-analysis" was included for databases with no predefined search filter for review articles. No language restrictions were applied (**Appendix *2***).

3.3.4 SRs selection process

The publications retrieved from the searches were combined into one library in EndNote X8 (Clarivate Analytics, Philadelphia, US). Duplicates were removed. A manual search was performed on the bibliographies of these retrieved publications to identify further reviews to be assessed. Screening of the titles and abstracts was carried out independently and in duplicate by two authors and assessed against inclusion and exclusion criteria. All publications assessed as potentially eligible at this stage were included for the next round of screening.

Full texts of those were retrieved and two reviewers screened the publications independently and in duplicate to assess eligibility. Where there were discrepancies, a third reviewer was consulted, and discussion took place before making a final decision.

3.3.5 Data collection and synthesis

To minimise the risk of bias, a standardised data extraction tool was used to develop a proforma (**Appendix *3***). This was developed *a priori* and pilot tested on one of the included SRs. It was then employed by two reviewers to independently extract data from each included SR. Root caries SRs and coronal caries SRs were analysed separately because their target populations were different. Root caries studies focused on older adults and coronal caries studies on children. The SRs included different studies with no studies shared between them. For SRs investigating other interventions alongside SDF, only SDF data were considered.

Guided by the proforma, information extracted from each included SR included the following:

1- Citation and funding details;
2- Objectives of the included SR;
3- Search strategy;
4- PICO items;
5- Instruments used to appraise the primary studies or grade the quality of evidence;
6- Method of synthesis/analysis employed to synthesis the evidence;

7- Number of studies, countries of origin of studies included in the SR and publication date range for studies included in the SR;
8- SR authors' stated limitations and conclusions;
9- Adverse events, if reported, and
10- Umbrella review authors' additional comments.

The breadth of evidence and adverse events assessed in the SRs were summarised narratively through data tables of the SRs' characteristics. To analyse the effectiveness of SDF for managing carious lesions, similar outcome measures and comparator interventions were brought together to allow their synthesis and/ or comparison and to identify where it might be possible to carry out meta-analyses.

3.3.6 Analysis of the degree of overlap in studies

It is recommended that umbrella reviews should analyse the degree of overlap in primary studies across SRs where appropriate (Pieper et al., 2014a). It is expected that in SRs focussing on the same topic, multiple primary studies will be included in more than one SR, and a certain degree of overlap in primary studies will appear. To determine the degree of this overlap in the primary studies, citation matrices presenting all the included SRs and primary publications were generated and "Corrected Covered Areas" (CCAs) were calculated (Pieper et al., 2014a). This requires identifying the unique primary studies (the first occurrence of primary studies) appeared across the SRs, which is referred to as index publications.

CCA was calculated to measure overlap by dividing the total number of primary studies (including double counting) included in all SRs reduced by the number of unique primary studies, by the product of the number of unique primary studies (rows) and the number of SRs (columns), and this product is reduced by the number of unique primary studies. This reduction results in a range of (0-100%) for the CCA for each citation matrix. CCA= 0-5; slight, 6-10; moderate, 11-15; high, and >15; very high overlap of primary studies across SRs (Figure 3-2). CCA was calculated separately for SRs dealing with coronal caries and SRs dealing with root caries.

	SR 1	SR 2	SR 3
Primary publication 1	x		
Primary publication 2	x		x
Primary publication 3	x	x	x
Primary publication 4		x	
Primary publication 5		x	x

Citation matrix

$$CA\ (covered\ area) = \frac{N}{rc}$$

$$CCA\ (Corrected\ CA) = \frac{N - r}{rc - r}$$

Where N is the number of included publications (including double counting), in evidence synthesis (this is the sum of ticked boxes in the citation matrix); where r is the number of rows (number of index publications) and c is the number of columns (number of reviews).

Figure 3-2 Citation matrix and calculation formulas. CA, covered area; CCA, corrected covered area (Reproduced with the author's permission) (Pieper et al., 2014a)

3.3.7 Assessing SRs' risk of bias

Two reviewers assessed risk of bias within the SRs independently, and in duplicate, using Risk Of Bias In Systematic reviews (ROBIS) (**Appendix *4***). Scoring discrepancies were resolved through discussion until consensus was reached. Authors were contacted where clarification was required. The ROBIS tool assesses the SR across three phases (Whiting et al., 2016);

3.3.7.1 Relevance of the SR

This was assessed by comparing Participant, Intervention, Comparator and Outcome (PICO) items of the SRs and those of the umbrella review to ensure that the research questions of the two reviews match.

3.3.7.2 Identifying concerns within the SR process

This aims to identify whether bias may have occurred during any stage of the SR, which helps to judge the risk of bias in the final phase. The signalling questions are answered as “Yes”, “Probably Yes”, “Probably No”, “No” and “No Information”, with “No” indicating high concerns. These are then considered together to give a “low”, “high” or “unclear” concern. The evaluation involves four domains to ensure covering main SR processes;

Study eligibility criteria

This domain aims to evaluate whether there were pre-specified appropriate inclusion criteria. Ideally every SR should refer and adhere to a priori registered protocol to ensure consistency through the primary studies inclusion process rather than the on the characteristics and results of the primary studies.

Identification and selection of studies

The second domain aims to assess whether the SR might have excluded any primary studies that would have met the inclusion criteria. A thorough and comprehensive search strategy to identify published and unpublished primary studies is a crucial part of any SR. Moreover, additional search methods should help identify further potential eligible reports. Independent and in duplicate

studies selection by two authors help to ensure that all eligible studies are included in the SRs.

Data collection and study appraisal

The *a priori* piloted data extraction tool should have been developed during the protocol stage. The data extraction tool should include characteristics and results of the primary studies; study design feature, PICO items, funding sources numerical and statistical data etc. Similar to studies selection, data collection and study appraisal should be conducted by two authors independently and in duplicate to ensure accuracy of the results.

3.3.7.3 Synthesis and findings

The final domain aims to evaluate whether the results synthesis approach followed (qualitative or quantitative) was appropriate. Justification for the method followed should be provided depending on the nature of the SR question and included primary studies.

3.3.7.4 Judging risk of bias

The final phase assesses the SR as a whole and the degree to which it is at risk of bias. The evaluation process including the signalling questions is similar to the one in the previous domain. However, an overall judgment of risk of bias is recorded rather than the concern about bias.

3.4 Results

Figure 3-3 shows the flow diagram of the identification and selection of SRs process. The initial searches yielded 41 potential eligible reviews (Embase n=17, PubMed n=23, Cochrane Database of SRs n=1). The search in the PROSPERO register retrieved six ongoing, unfinished reviews, which were excluded. However, it appears later that two of them have been actually finished and published but their statuses had not been updated in PROSPERO, but these were also retrieved from the other databases and included in the umbrella review. No SRs were found in Joanna Briggs Institute Database of SRs and Implementation papers.

All studies retrieved were reported in English. Among these 41 reviews, 12 were identified as duplicates and removed resulting in a total of 29 reviews. In addition, four potential publications were identified from searching bibliographies (Weyant et al., 2013, Wierichs and Meyer-Lueckel, 2015, Gao et al., 2016b, Mei et al., 2016). The searches therefore identified 33 potentially eligible reviews for inclusion.

Following the screening of titles and abstracts by two reviewers independently and in duplicate, 14 reviews were excluded. The full texts of the remaining 19 reviews were retrieved and assessed, again by two independent reviewers. Based on this, eight reviews were excluded because they were not SRs (Chu and Lo, 2008, Fung et al., 2013, Horst et al., 2016) or did not include SDF or address its arresting or preventing dental caries (Weyant et al., 2013, Twetman and Dhar, 2015, Schwendicke and Göstemeyer, 2017). Authors of two reviews were contacted for missing information but did not respond within the study timeframe,

these studies were also excluded (Peng et al., 2012, Sharma et al., 2015). This resulted in 11 papers that met the inclusion criteria.

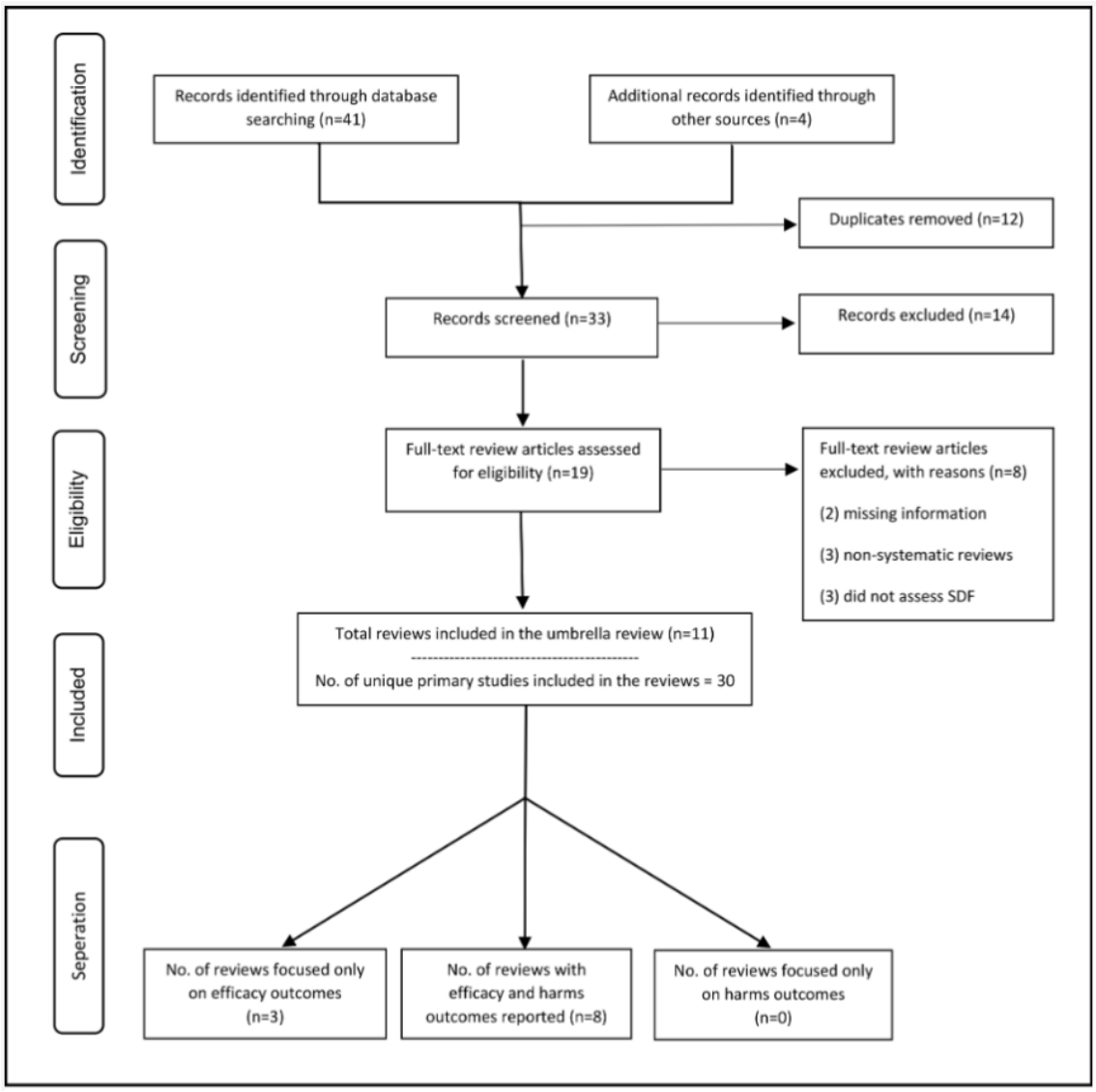

Figure 3-3 Flow diagram of SRs identification and selection process

3.4.1 Breadth and comprehensiveness of the evidence

The 11 SR papers reported 63 primary studies; 30 of which were identified as unique publications (26 studies were concerned with coronal caries and four studies with root caries). Four SRs focussed on root caries (Gluzman et al., 2013, Wierichs and Meyer-Lueckel, 2015, Hendre et al., 2017, Oliveira et al., 2018) and seven on coronal caries (Rosenblatt et al., 2009, Duangthip et al., 2015, Gao et

al., 2016b, Gao et al., 2016a, Chibinski et al., 2017, Contreras et al., 2017, Oliveira et al., 2019). Characteristics of the SRs and their included studies are summarised below.

3.4.1.1 Characteristics of the SRs

Characteristics of each SR are presented in Table 3-1 and Table 3-2. Summary of SRs characteristics is presented below.

Search period and strategies:

Four SRs did not impose restrictions on the date of the start-up of the search with end date of the search being 2017 in two SRs (Oliveira et al., 2018, Oliveira et al., 2019) and 2016 in two SRs (Gao et al., 2016b, Chibinski et al., 2017). However, the start-up date of the search for four SRs was the late 1940s, with the end date being to 2014 in three SRs (Duangthip et al., 2015, Wierichs and Meyer-Lueckel, 2015, Gao et al., 2016a) and 2015 in one SR (Hendre et al., 2017). The search timeframes for the other three SRs were narrower; 1966-2006 (Rosenblatt et al., 2009), 1979-2010 (Gluzman et al., 2013) and 2005-2016 (Contreras et al., 2017).

PubMed/Medline, the Cochrane library and Embase databases were the most common ones searched; in 11, 9, 8 SRs respectively. Other databases sourced included; Scopus (n=4), the Latin American and Caribbean Health Sciences Literature database LILACS (n=4), Biblioteca Brasileira de Odontologia BBO (n=4), Web of Science (n=4), SciELO (n=2), Google Scholar (n=2), Science Direct (n=1), China National Knowledge Infrastructure (n=1), Ichushi-web (n=1), Biblioteca Virtual en Salud Espana (n=1) and Biblioteca Virtual em Saude (n=1)

and the American Dental Association's Evidence-Based Dentistry Website and repository of the Journal (n=1).

One SR explored the grey literature, using Google Scholar and the database system for information on grey literature in Europe and it searched for dissertations and theses using the ProQuest Dissertations and Theses Full Text databases and the Periodicos Capes Theses database (Chibinski et al., 2017).

Two SRs searched five registries of ongoing trials; ClinicalTrials.gov, Brazilian Clinical Trials Registry, European Union Clinical Trials register, International Standard Randomised Controlled Trial Number Registry and Current Controlled Trials, and Australian New Zealand Clinical Trials Registry, and the Brazilian database of theses and dissertations (Oliveira et al., 2018, Oliveira et al., 2019).

Only three SRs did not impose any language restrictions (Chibinski et al., 2017, Oliveira et al., 2018, Oliveira et al., 2019). Language was restricted to English in five SRs (Gluzman et al., 2013, Duangthip et al., 2015, Gao et al., 2016a, Contreras et al., 2017, Hendre et al., 2017), one systematic included English, Spanish and Portuguese (Rosenblatt et al., 2009), one systematic included English and German (Wierichs and Meyer-Lueckel, 2015) and one included Japanese, Chinese, English, Portuguese and Spanish (Gao et al., 2016b).

Participants:

Six SRs considered children only in their inclusion criteria (Duangthip et al., 2015, Gao et al., 2016b, Gao et al., 2016a, Chibinski et al., 2017, Contreras et al., 2017, Oliveira et al., 2019), whereas, one SR did not specify an age group and looked at “humans” (Rosenblatt et al., 2009). Two SRs were restricted to older adults (Gluzman et al., 2013, Hendre et al., 2017) while two SRs were more strict,

including adults with exposed root surface (Wierichs and Meyer-Lueckel, 2015, Oliveira et al., 2018).

Interventions:

Seven SRs included SDF of any concentration (Rosenblatt et al., 2009, Gao et al., 2016b, Chibinski et al., 2017, Contreras et al., 2017, Hendre et al., 2017, Oliveira et al., 2018, Oliveira et al., 2019). However, four SRs included other agents in addition to SDF such as chlorhexidine, xylitol, sealants, saliva stimulators, and other fluoride agents (Gluzman et al., 2013, Duangthip et al., 2015, Wierichs and Meyer-Lueckel, 2015, Gao et al., 2016a).

Comparators:

Six SRs did not specify a comparison to the intervention (Gluzman et al., 2013, Duangthip et al., 2015, Gao et al., 2016b, Gao et al., 2016a, Contreras et al., 2017, Hendre et al., 2017). However, four SRs included studies comparing the intervention to no treatment, placebo or other intervention(s) (Wierichs and Meyer-Lueckel, 2015, Chibinski et al., 2017, Oliveira et al., 2018, Oliveira et al., 2019). One SR compared SDF to FV (Rosenblatt et al., 2009).

Outcomes and outcomes measures:

Of the four SRs that investigated root caries, one SR focused on carious lesions prevention only (Gluzman et al., 2013), two SRs explored carious lesion prevention and arrest (Oliveira et al., 2018, Wierichs and Meyer-Lueckel, 2015) and, in addition to root carious lesion prevention and arrest, one SR investigated SDF on coronal carious lesions in adults, but failed to retrieve any studies investigating the effect of SDF on coronal caries in adults (Hendre et al., 2017).

Seven SRs investigated the effect of the intervention on coronal carious lesions with four SRs focussing on carious lesion arrest (Duangthip et al., 2015, Gao et al., 2016b, Gao et al., 2016a, Chibinski et al., 2017), one SR centred only on carious lesion prevention and two SRs investigated both carious lesion prevention and arrest. Eight SRs reported adverse events associated with SDF treatment (Rosenblatt et al., 2009, Duangthip et al., 2015, Gao et al., 2016b, Gao et al., 2016a, Contreras et al., 2017, Hendre et al., 2017, Oliveira et al., 2018, Oliveira et al., 2019).

For measuring SDF effectiveness in preventing and arresting carious lesions, the SRs used six different outcome measures: % success rates (n=4); prevented fraction PF (n=4); number needed to treat NNT (n=2) ; weighted mean difference WMD (n=2); mean difference MD (n=1) and risk ratio RR (n=1). The outcome measurement was not clear in one SR that did not synthesise results from included studies but presented the original reported data (Contreras et al., 2017).

Results synthesising:

Five of the SRs used a narrative approach, as they were unable to quantitatively synthesise the results (Rosenblatt et al., 2009, Gluzman et al., 2013, Duangthip et al., 2015, Contreras et al., 2017, Hendre et al., 2017). Six SRs reported carrying out a meta-analysis to synthesize the findings (Wierichs and Meyer-Lueckel, 2015, Gao et al., 2016a, Gao et al., 2016b, Chibinski et al., 2017, Oliveira et al., 2018, Oliveira et al., 2019).

Evaluating primary studies and quality of evidence:

Eight SRs used the Cochrane risk of bias assessment tool or a simplified analysis adapted from recommendations in the Cochrane Handbook of SRs of Interventions to appraise the quality of included studies (Duangthip et al., 2015, Wierichs and Meyer-Lueckel, 2015, Gao et al., 2016b, Gao et al., 2016a, Chibinski et al., 2017, Contreras et al., 2017, Oliveira et al., 2018, Oliveira et al., 2019). One SR used Jadad, 1998 (Rosenblatt et al., 2009), and another SR used the critical appraisal worksheet for RCTs from the Oxford Centre for Evidence-Based Medicine CEBM 2005 (Hendre et al., 2017). However, one SR did not evaluate the included studies at all (Gluzman et al., 2013). In order to appraise the quality of evidence, two used Grading of Recommendations, Assessment, Development and Evaluations (GRADE) (Wierichs and Meyer-Lueckel, 2015, Chibinski et al., 2017).

Table 3-1 Characteristics of root caries SRs

Authors/ Title-year/ Citation/Funding source	Aim	Search strategy	Participants	Interventions	Comparators	Outcomes	Meta-analysis	Instruments used to appraise studies/evidence
R. Gluzman, R.V Katz, B.J. Frey, R. McGowan **Prevention of root caries: a literature review of primary and secondary preventive agents. 2013** Spec Care Dentist 33(3): 133-140 *The American Dental Association and The National Institute for Dental Craniofacial Research at NIH*	"To summarize the effectiveness of seven leading root caries preventive agents and provide recommendations for use of those agents in clinical practice with older adults and vulnerable elderly."	***Databases:*** PubMed/Medline and Cochrane Library ***Other approaches:*** Reviewing reference lists and search for the most recent publications in main dental journals to compensate for the delay in transfer to electronic database ***Search period:*** Jan 1979 – Jul 2010 ***Language restriction:*** *Only English papers were included*	Older adults	Fluoride, chlorhexidine, xylitol, amorphous calcium phosphate, sealants, saliva stimulators, and SDF.	Not stated	**Outcomes:** Reduction in root caries incidence or root caries arrest **Outcomes measurement:** The percentage reduction in root caries was calculated.	No	There was no assessment of the quality of included studies
R.J. Wierichs, H. Meyer-Lueckel **SR on non-invasive treatment of root caries lesions. 2015** Journal of Dental Research, Vol. 94(2) 261-271 *The authors and their institution (RWTH Aachen University)*	"To systematically retrieve and analyse clinical studies investigating chemical agents to reduce the initiation of root caries lesion and/or increase their inactivation."	***Databases:*** PubMed, EMBASE, and Cochrane Library ***Other approaches:*** Cross-referencing ***Search period:*** Jan 1947- May 2014 ***Language restriction:*** English and German papers were included	"Humans who retained a minimum of 1 natural tooth with exposed root surfaces with or without root caries lesions"	Preventive dental regimes (e.g., oral health instruction) and/or 1 or more chemical agents applied on 1 or more occasion by a dental professional or self-applied by the patient.	placebo, positive interventions, e.g., Duraphat varnish), or standard therapy"	**Outcomes:** Clinical or radiographic visible changes of active or inactive root caries. **Outcomes measurement:** Mean differences were calculated for changes in DMFRS/DFRS	Yes	Cochrane risk of bias assessment tool. The quality of the evidence was evaluated using the GRADE approach. Publication bias was assessed by funnel plots.
A.D Hendra, G.W. Taylor, E.M. Chavez, S. Hyde **A SR of silver diamine fluoride: Effectiveness and application in older adults. 2017** Gerodontology; 34:411-419 *An unrestricted honorarium from the American Dental Association's National Elder Care Advisory Committee of the Council on Access, Prevention and Interprofessional Relations*	"To examines the effectiveness of silver diamine fluoride (SDF) in the management of caries in older adults."	***Databases:*** PubMed, PubMed Clinical Queries, EMBASE, the American Dental Association's Evidence-Based Dentistry Website, Cochrane Library, Web of Science, repository of the Journal of the American Dental Association and Google Scholar. ***Other approaches:*** Hand search of bibliographies ***Search period:*** 1946 to November 2015 with monthly reruns of search terms in PubMed through August 2016: ***Language restriction:*** Only English papers were included	Adults	SDF	Not stated	**Outcomes:** Caries prevention, arrest or remineralization. **Outcomes measurement:** The effectiveness of SDF was measure using the following parameters: NNT, PF, relative risk, arrest rate and mean number of new carious surfaces and mean number of arrested root surfaces.	No	The critical appraisal worksheet for RCTs from the Oxford CEBM provided the framework to assess the quality and risk of bias of the selected articles.

Authors/ Title-year/ Citation/Funding source	Aim	Search strategy	Participants	Interventions	Comparators	Outcomes	Meta-analysis	Instruments used to appraise studies/evidence
B.H Oliveira, J. Cunha-Cruz, A. Rajendra, R. Niederman **Controlling caries in exposed root surfaces with silver diamine fluoride: A SR with meta-analysis. 2018** J Am Dent Assoc.149(8):671-679. *The National Institute on Minority Health and Health Disparities of the National Institutes of Health, and partially funded through a Patient-Cantered Outcomes Research Institute Award. The Teacher Training Program of the University of the State of Rio de Janeiro also supported this work.*	"To assess the effect of SDF in preventing and arresting caries in exposed root surfaces of adults."	***Databases:*** Cochrane Library, Embase, MEDLINE via PubMed, Scopus, Web of Science, LILACS, BBO, SciELO, Clinical Trials.gov, Brazilian Clinical Trials Registry, European Union Clinical Trials Register, International Standard Randomised Controlled Trials Registry and Current Controlled Trial, Australian New Zealand Clinical Trials Registry and Brazilian database of theses and dissertation ***Other approaches:*** Cross-referencing from narrative reviews ***Search period:*** No date restrictions to start up to July 2017. ***Language restriction:*** No restrictions	Adults with exposed root surfaces	SDF	No intervention, placebo, or any cariostatic agent or restorative material	**Outcomes:** Primary outcome: development of new carious lesions and arrest of existing carious lesions in exposed root surfaces of permanent teeth within at least 12 months after produce application Secondary outcome: any self-reported, caregiver-reported, or professionally diagnosed adverse events. **Outcomes measurement:** For caries prevention, the difference in mean caries increment between SDF and control groups, PFs were calculated. For caries arrest, the difference in mean numbers of arrested lesions between SDF and control groups.	Yes	Cochrane risk of bias assessment tool

Table 3-2 Characteristics of coronal SRs

Authors/ Title-year/ Citation/Funding source	Aim	Search strategy	Participants	Interventions	Comparators	Outcomes	Meta-analysis	Instrument used to appraise studies/evidence
A. Rosenblatt, T.C.M. Stamford, R. Niederman **Silver diamine fluoride: a caries "silver-fluoride bullet". 2009** J Dent Res 88(2):116-125. *The Fulbright Program and The Forsyth Institute*	"Will SDF more effectively prevent caries than fluoride varnish?"	***Databases:*** MEDLINE, LILACS, EMBASE, the Cochrane Library, and BBO ***Other approaches:*** Reviewing reference lists ***Search period:*** 1966 - Dec 31, 2006 ***Language restriction:*** English, Spanish, or Portuguese papers were included	"Humans"	SDF	FV	**Outcomes:** Although the research question is about prevention, the study reported both caries prevention and arrest **Outcomes measurement:** PF and NNT were calculated from the original data.	No	Jadad, 1998
D. Duangthip, M. Jiang, C.H. Chu, E.C.M. Lo **Non-surgical treatment of dentin caries in preschool children – SR. 2015** BMC Oral Health15:44 *Faculty of Dentistry, University of Hong Kong*	"To systematically review and evaluate the literature on the effectiveness of non-surgical methods in arresting or slowing down the progression of active dentine caries in primary teeth in preschool children."	***Databases:*** PubMed, Cochrane Library, and EMBASE ***Other approaches:*** None ***Search period:*** 1947- Jun 2014 ***Language restriction:*** Only English papers were included	"Children aged 6 or below who had at least one dentin carious lesion in the primary dentition"	nonsurgical interventions such as fluoride agents, dental sealant, ozone and oral health education	Not stated	**Outcomes:** Caries arrest, progression or regression. There could be comparisons of outcomes of different nonsurgical approaches, or nonsurgical and surgical approaches **Outcomes measurement:** Not clear, but the primary summary measure for reporting in this review was success rates of various treatments.	No	Cochrane risk of bias assessment tool Graded for quality using ADA criteria
S.S. Gao, I.S. Zhao, N. Hiraishi, D. Duangthip, M.L. Mei, E.C.M. Lo, C.H. Chu **Clinical trials of silver diamine fluoride in arresting caries among children: a SR. 2016** JDR Clinical & Transitional Research, Vol 1, Issue 3, page(s): 201-210 *The General Research Fund of the University Grant Council, Hong Kong*	"To investigate the clinical effectiveness of SDF in arresting dental caries among children."	***Databases:*** PubMed, EMBASE, Scopus, China National Knowledge Infrastructure, Ichushi-web, Biblioteca Virtual en Salud Espana and Biblioteca Virtual em Saude ***Other approaches:*** Manual screening of the bibliographies ***Search period:*** No limit, the last search was made in Mar 2016 ***Language restriction:*** English, Chinese, Japanese, Portuguese and Spanish papers were included	Children (primary and permanent teeth)	SDF	With or without control group	**Outcomes:** Carries arrest **Outcomes measurement:** The percentage of dental caries that had become arrested after SDF treatment was calculated if possible. Otherwise, the original data were reported	Yes	"Risk of bias was assessed for each included study from 6 aspects: 1) random sequence generation (selection bias), 2) allocation concealment (selection bias), 3) blinding of outcome assessment (detection bias), 4) incomplete outcome data (attrition bias), 5) selective reporting (reporting bias), and 6) other bias."

Authors/ Title-year/ Citation/Funding source	Aim	Search strategy	Participants	Interventions	Comparators	Outcomes	Meta-analysis	Instrument used to appraise studies/evidence
S.S. Gao, S. Zhang, M.L. Mei, E.C.M. Lo, C.H. Chu **Caries remineralisation and arresting effect in children by professionally applied fluoride treatment – a SR. 2016** BMC Oral Health 16:12 *The General Research Fund of the University Grant Council, Hong Kong*	"To investigate the clinical efficacy of professional fluoride therapy in remineralising and arresting caries in children."	***Databases:*** PubMed, Cochrane Library, ISI Web of Science and EMBASE ***Other approaches:*** Manual screening of the bibliographies ***Search period:*** 1948 - 2014 ***Language restriction:*** Only English papers were included	Children (primary and permanent teeth)	Silicon tetrafluoride, fluoride gel, SDF, sodium fluoride or nano-silver fluoride	Not stated	**Outcomes:** The remineralisation or arresting effect of caries by professional fluoride treatment. **Outcomes measurement:** The percentage of remineralised early enamel caries and the percentage of arrested dentine caries were calculated.	Yes	Cochrane risk of bias assessment tool
V. Contreras, M.J Toro, A.R. Elias-Boneta, A. Encarnacion-Burgos **Effectiveness of silver diamine fluoride in caries prevention and arrest: a systematic literature review. 2016** AGD; No. 402, p. 30 *National Institutes of Health and the National Institute on Minority Health and Health Disparities*	"Is the use of SDF more effective than other strategies in the prevention and/or arrest of carious lesions in children who have caries in primary teeth and/or permanent first molars?"	***Databases:*** PubMed, Science Direct and Scopus ***Other approaches:*** *None* ***Search period:*** Aug 2005 – Jan 2016 ***Language restriction:*** Only English papers were included	Children (primary and permanent teeth)	SDF	Not stated	**Outcomes:** Mean number of surfaces with new, active, and inactive caries at baseline and follow-up; mean numbers of arrested surfaces; the percentage of caries arrest; and caries increment **Outcomes measurement:** Not clear. Only the original data was reported.	No	Risk of bias was assessed using a simplified analysis adapted from the recommendations in the Cochrane Handbook of SRs of Interventions

Authors/ Title-year/ Citation/Funding source	Aim	Search strategy	Participants	Interventions	Comparators	Outcomes	Meta-analysis	Instrument used to appraise studies/evidence
A.C. Chibinski, L. M. Wambier, J. Feltrin, A.D Loguercio, D.S Wambier, A. Reis **Silver Diamine Fluoride Has Efficacy in Controlling Caries Progression in Primary Teeth: A SR and Meta-Analysis. 2017** Caries Res; 51:527-541 *The National Council for Scientific and Technological Development*	"To evaluate the efficacy of silver diamine fluoride (SDF) in controlling caries progression in children when compared with active treatments or placebos."	***Databases:*** PubMed, Scopus, Web of Science, LILACS, BBO and the Cochrane Library. The grey literature was explored using the database System for Information on Grey Literature in Europe and Google Scholar. Dissertations and theses were searched using the ProQuest Dissertations and Theses Full Text databases and the Periodicos Capes Theses database. ***Other approaches:*** Hand search of reference lists ***Search period:*** No restrictions ***Language restriction***: No restrictions	Children (primary and permanent teeth)	SDF	placebo or other active treatments	**Outcomes:** The arrestment of the carious lesion in enamel or dentin. **Outcomes measurement:** The outcomes were summarized by calculating the risk ratio and the 95% confidence interval	Yes	Cochrane risk of bias assessment tool. The quality of the evidence was evaluated using the GRADE approach.
B.H Oliveira, A. Rajendra, A.V Keenan, R. Niederman **The Effect of Silver Diamine Fluoride in Preventing Caries in the Primary Dentition: A SR and Meta-Analysis. 2018** Caries Res; 6;53(1):24-32 *The National Institute on Minority Health and Health Disparities of the National Institutes of Health and, and partially funded through a Patient-Cantered Outcomes Research Institute. The Teacher Training Program of the University of the State of Rio de Janeiro also supported this work.*	"To investigate whether silver diamine fluoride (SDF) is effective in preventing new caries lesions in primary teeth when compared to placebo or active treatments."	***Databases:*** Cochrane Library, Embase, MEDLINE via PubMed, Scopus, Web of Science, LILACS, BBO, SciELO, Clinical Trials.gov, Brazilian Clinical Trials Registry, European Union Clinical Trials Register, International Standard Randomised Controlled Trials Registry and Current Controlled Trial, Australian New Zealand Clinical Trials Registry and Capes Dissertations database ***Other approaches:*** Cross-referencing from narrative reviews ***Search period:*** No date restrictions to start up to July 2017. ***Language restriction:*** No restrictions	Children (Primary teeth)	SDF	No intervention, placebo, any topical cariostatic agents, resin or glass ionomer pit and fissure sealants or dental restorative materials;	**Outcomes:** Primary outcome: the development of new dentin caries lesions at surface, tooth, or patient level. Secondary outcome: any self/parent-reported or professionally diagnosed adverse events. **Outcomes measurement:** The difference in mean caries increment between SDF and control groups, PFs were calculated.	Yes	Cochrane risk of bias assessment tool

3.4.1.2 Characteristics of the studies included in SRs

Number, type and quality of the studies included in SRs:

The number of included SDF studies varied widely across the SRs; three SRs included one or two RCTs, while others included seven studies or more (Rosenblatt SR included the study by Chu et al (2002) as a cohort design, while it was included as an RCT in other SRs). Gao included seven RCTs dealing with SDF in one SR and 19 prospective clinical trials in another SR, without further clarifying whether they were RCTs or not (seven of them were identified as RCTs by cross referencing against other included SRs). The root caries studies included in the SRs were of high quality and at low risk of bias, while for coronal caries studies; the reliability of those conducted before 2002 was relatively low, while studies after that were of better quality.

Countries of origin:

Authors of five SRs did not state the country of origin of included studies (Rosenblatt et al., 2009, Gluzman et al., 2013, Wierichs and Meyer-Lueckel, 2015, Gao et al., 2016a, Chibinski et al., 2017). However, these could be identified by cross-referencing against other included SRs or by going back to the individual studies. Most SDF studies were conducted in China and Brazil, with seven studies in each, while five and four studies were identified in Hong Kong and Japan, respectively. One study was conducted in each of the following countries: Nepal, Philippines, Cuba, Argentina, and Turkey.

Publication date range:

It is noteworthy that the first study assessing the effectiveness SDF was published in 1969 (Nishino, 1969) and only one SR retrieved studies published

before 2001 (Gao et al., 2016b), while the rest of the SRs only retrieved studies published after 2002.

3.4.2 Analysis of the degree of overlap in studies

3.4.2.1 Root caries SRs

Citation matrix was generated for root caries SRs (Figure 3-4). CCA was then calculated as the following:

$$CCA = \frac{N - r}{rc - r} = \frac{10 - 4}{16 - 4} = \frac{6}{12} = 0.5$$

CCA= 0.5, this means that the degree of overlap is 50% (>15) and therefore the degree of overlap in studies across root caries SRs is very high.

	Gluzman et al., 2013	Wierichs et al., 2015	Hendre et al., 2017	Oliveira et al., 2018
Tan et al., 2010	X	X	X	X
Zhang et al,.2013		X	X	X
Li et al ,2016			X	X
Li et al ,2017				X

Figure 3-4 Citation matrix for root caries SRs

3.4.2.2 Coronal caries SRs

Citation matrix was generated for coronal caries SRs (Figure 3-5). CCA was then calculated as the following:

$$CCA = \frac{N - r}{rc - r} = \frac{54 - 27}{182 - 27} = \frac{27}{155} = 0.17$$

CCA= 0.17, this means that the degree of overlap is 17% (>15) and therefore the degree of overlap in studies across coronal caries SRs is very high.

	Rosenblatt et al., 2009	Duangthip et al., 2015	Gao et al., 2016a	Gao et al., 2016b	Contreras et al., 2017	Chibinski et al., 2017	Oliveira et al., 2019
Nishino et al.,1969			X				
Yoshida et al., 1976			X				
Tsutsumi et al., 1981			X				
Wang, 1984			X				
Oliveira, 1985			X				
Maciel, 1988			X				
Bijella, 1991							X
Ye, 1995			X				
Miasato, 1996			X				
Fukumoto et al., 1997			X				
Lo et al., 2001				X			
Yang et al., 2002			X				
Chu et al., 2002	X	X	X	X		X	X
Mauro et al., 2004			X				
Llodra et al., 2005	X		X	X	X	X	X
Huang et al., 2006			X				
Braga et al., 2009			X	X	X		
Yee et al., 2009			X	X	X	X	
Vasconcelos, 2011						X	
Monse et al., 2012					X	X	
Liu et al., 2012						X	
Zhi et al., 2012		X	X	X	X	X	X
dos Santos et al., 2012		X	X	X	X	X	
Seberol and Okte, 2013						X	
Dos santos et al., 2014						X	
Duangthip et al., 2016			X		X	X	

Figure 3-5 Citation matrix for coronal caries SRs

3.4.3 Assessing SRs risk of bias

3.4.3.1 Root caries SRs' risk of bias

Using the ROBIS tool to assess risk of bias (Whiting et al., 2016), three SRs to be at high risk of bias (Gluzman et al., 2013, Wierichs and Meyer-Lueckel, 2015, Hendre et al., 2017), and one SR at low risk of bias (Oliveira et al., 2018), which was assessed as having low concern for bias across all stages of the SR process, starting from study eligibility, identification and selection of studies, data collection and study appraisal, and ending with synthesis and findings. All SRs questions were assessed as relevant to the umbrella review question Table 3-3.

Study eligibility criteria

Eligibility criteria for the SR question were appropriate for the four SRs. However, as SDF is popular in non-English speaking countries and studies might have been often reported in non-English journals, limiting to English language reduced the comprehensiveness of the primary studies that were retrieved from searching and included. This immediately placed significant bias within those two SRs (Gluzman et al., 2013, Hendre et al., 2017). In addition, absence of an *a priori* research protocol affected the risk of bias score for three SRs (Gluzman et al., 2013, Wierichs and Meyer-Lueckel, 2015, Hendre et al., 2017).

Identification and selection of studies

In addition to the language restriction in two SRs (Gluzman et al., 2013, Hendre et al., 2017), It was unclear in one SR whether the study selection process had been undertaken independently and in duplicate by two reviewers (Hendre et al., 2017). Three SRs searched a wide range of databases (Wierichs and Meyer-

Lueckel, 2015, Hendre et al., 2017, Oliveira et al., 2018). However, (Gluzman et al., 2013) searched only two databases; PubMed and Cochrane Library.

Data collection and study appraisal

It was unclear in one SR whether their studies' data collection processes had been undertaken independently, by at least two reviewers (Hendre et al., 2017). One SR did not appraise the included studies which placed significant bias within this SR (Gluzman et al., 2013). Three SRs appraised studies using acceptable approaches (Wierichs and Meyer-Lueckel, 2015, Hendre et al., 2017, Oliveira et al., 2018). However, it was unclear in one SR if this has been carried out independently by two reviewers (Wierichs and Meyer-Lueckel, 2015).

Synthesis and findings

All SRs used appropriate analytical approaches and heterogeneity across studies was taken into account. However, not having an *a priori* designed protocol affected the risk of bias in three SRs (Gluzman et al., 2013, Wierichs and Meyer-Lueckel, 2015, Hendre et al., 2017), since there was no indication that predefined analyses were followed.

Table 3-3 Root caries SRs risk of bias (ROBIS)

Systematic review	ROBIS					
	Assessing relevance	Review process				Risk of bias
		Study eligibility criteria	Identification and selection of studies	Data collection and study appraisal	Synthesis and findings	
Gluzman (2013)	√	⊖	⊕	⊖	●	⊖
Wierichs and Meyer-Lueckel (2015)	√	⊕	⊕	⊕	⊖	⊖
Hendre (2017)	√	⊖	⊖	⊕	⊕	⊖
Oliveira (2018)	√	⊕	⊕	⊕	⊕	⊕

3.4.3.2 Coronal caries SRs' risk of bias

Using the ROBIS tool to assess risk of bias (Whiting et al., 2016), two SRs were found to be at high risk of bias (Rosenblatt et al., 2009, Duangthip et al., 2015), and four at low risk of bias (Gao et al., 2016b, Gao et al., 2016a, Chibinski et al., 2017, Oliveira et al., 2019), whilst the risk of bias was unclear for one SR (Contreras et al., 2017). Two SRs were assessed as having low concern for bias across all stages of the SR process, starting from study eligibility, identification and selection of studies, data collection and study appraisal, and ending with synthesis and findings (Chibinski et al., 2017, Oliveira et al., 2019). All SRs questions were assessed as relevant to the umbrella review question Table 3-4.

Study eligibility criteria

Eligibility criteria for the SR question were appropriate for the seven SRs. However, and similar to root caries SRs, limiting to English language reduced the comprehensiveness of the primary studies that were retrieved from searching and included. This immediately placed significant bias within those three SRs (Duangthip et al., 2015, Gao et al., 2016a, Contreras et al., 2017).

Only two SRs referred to having *a priori* research protocol (Chibinski et al., 2017, Oliveira et al., 2019), while it was not reported whether a *priori* research protocol was developed in the other five SRs (Rosenblatt et al., 2009, Duangthip et al., 2015, Gao et al., 2016b, Gao et al., 2016a, Contreras et al., 2017).

Identification and selection of studies

In addition to the language restriction in thee SRs (Duangthip et al., 2015, Gao et al., 2016a, Contreras et al., 2017), it was unclear that in two SR whether the study

selection process had been undertaken independently and in duplicate by two reviewers (Gao et al., 2016a, Contreras et al., 2017).

Two SRs did not report using any additional methods other than searching the specified database searching to identify additional reports. However, it was not clear whether this additional methods were employed but not reported or not employed in the first place (Duangthip et al., 2015, Contreras et al., 2017).

Data collection and study appraisal

It was unclear in two SRs whether their studies' data collection processes had been undertaken independently, by at least two reviewers (Gao et al., 2016a, Contreras et al., 2017). All SRs appraised the included studies using acceptable approaches. However, in two SRs, it was unclear if this has been carried out independently by two reviewers (Duangthip et al., 2015, Contreras et al., 2017).

Synthesis and findings

Most SRs used appropriate analytical approaches and heterogeneity across studies was taken into account. However, not having an *a priori* designed protocol affected the risk of bias, since there was no indication that predefined analyses were followed. An example of this was; including studies in the analysis that should have not been included, such Rosenblatt's SR, which included a study, comparing SDF to water, while the research question was "*Will silver diamine fluoride (SDF) more effectively prevent caries than fluoride varnish*?" had a negative effect on the risk of bias for this domain.

Table 3-4 Coronal caries SRs' risk of bias (ROBIS)

Systematic review	ROBIS					
		Review process				
	Assessing relevance	Study eligibility criteria	Identification and selection of studies	Data collection and study appraisal	Synthesis and findings	Risk of bias
Rosenblatt (2009)	√					
Duangthip (2015)	√					
Gao (2016a)	√					
Gao (2016b)	√					
Contreras (2017)	√					
Chibinski (2017)	√					
Oliveira (2019)	√					

3.4.4 Findings of the SRs

Findings of each SR, including their results and conclusions along with additional limitations identified are presented in Table 3-5 and Table 3-6.

Due to the extent of the heterogeneity in the SRs with respect to participants (children and adults), interventions (concentrations and frequencies), comparators (placebo, FV, GIC and ART) outcomes (root and coronal carious lesions prevention and arrest) and outcome measures (success rate, PF, MD, WMD, NNT and RR) it was not possible to pool the data and combine the results quantitatively using meta-analyses. However, the SRs' results were summarised by categorising similar interventions into comparison groups. This allowed an overview of the direction of effect and the relative magnitude of that effect where data were similar.

Table 3-5 Findings of root caries SRs

Systematic review	Included SDF studies*			Systematic review authors' stated limitations	Systematic review authors' stated conclusions	Umbrella review authors' additional limitations	Umbrella review authors' comments
	Number of studies sample size (range)	Countries of origin (number in each country)	Publication date range				
Gluzman (2013) **Prevention of root caries: a literature review of primary and secondary preventive agents**	1 306	Hong Kong (1)	2010	"For the primary prevention studies, the "depth" of evidence is "thin", since all six of the most effective primary prevention agents or combination of agents were each tested only in a single study."	"For the 1° prevention of root caries the recommended 'best choice' is the 38% SDF solution professionally applied annually"	No referral to a priori designed protocol. Language was limited to English. No appraisal for the quality of each individual study or table of the characteristics and summary of the included studies.	Combining the effectiveness for all these different approaches is a very crude way of doing it and the heterogeneity of the studies really limits the conclusion and there should be little confidence in the findings having it done by this way, but the authors have been tasked with coming up with recommendations and forced results from the paper. The evidence regarding the effectiveness of SDF on root caries is very thin; based on only one study.
Wierichs and Meyer-Lueckel (2015) **Systematic review on non-invasive treatment of root caries lesions**	2 572 (266-306)	Hong Kong (2)	2010-2013	"The low numbers of clinical trials for each agent, the high risk of bias within studies, and the limiting grade of evidence."	"SDF varnish may inactivate existing and/or reduce the initiation of root carious lesions. However, results should be interpreted with caution, due to the low numbers of clinical trials for each agent, the high risk of bias within studies, and the limiting grade of evidence"	No referral to a priori designed protocol. Language was limited to English and German. Although data were combined, both studies had different application frequencies. The authors mentioned that 11 studies were not sponsored by manufactures but it is not clear which ones were and which ones were not.	Only 2 English studies were included. Both showed effectiveness for root caries lesions arrest/prevention in favour of SDF. However, a definite conclusion could not be drawn based on 2 studies.

Systematic review	Included SDF studies*			Systematic review authors' stated limitations	Systematic review authors' stated conclusions	Umbrella review authors' additional limitations	Umbrella review authors' comments
	Number of studies sample size (range)	Countries of origin (number in each country)	Publication date range				
Hendre (2017) **A systematic review of silver diamine fluoride: Effectiveness and application in older adults.**	3 studies 895 (266-323)	Hong Kong (3)	2010-2016	"Our search for studies on SDF in older populations resulted in only 3 well-conducted randomised clinical trials on root caries."	"This SR evaluates the use of SDF for both root caries prevention and arrest in older adults. Existing reports of SDF trials support effectiveness in root caries prevention and arrest, remineralization of deep occlusal lesions and treatment of hypersensitive dentin."	No referral to a priori designed protocol. Language was limited to English. The authors did not declare that there was no conflict of interests. There were some differences in the placebos and the use of Oral Hygiene Instruction and Education, application frequencies.	Dentin hypersensitivity is brought into the conclusions but has not been included in the search. The authors mentioned in the discussion that they expanded their search to include SDF safety, remineralization, and desensitization studies in adults but there are no details given on this in the paper. The authors reported the differences of effect sizes independently for each study and did not attempt to combine them into an overall effect size. This was likely to be appropriate because of the study duration, differences in placebos.
Oliveira (2018) **Controlling caries in exposed root surfaces with silver diamine fluoride: A SR with meta-analysis**	3 895 (266-323)	Hong Kong (3)	2010-2017	"The low number of clinical trials in which the investigators addressed our research question." "All included trials were from the same group of investigators and enrolled Chinese older adults with a low risk of developing caries." "We encountered moderate to considerable statistical heterogeneity when we pooled the WMDs."	"Yearly 38% SDF applications to exposed root surfaces of older adults are effective against caries initiation and progression. The preventive effect is similar to that of 5% FV and 1% chlorohexidine varnish. Further research is needed to replicate these findings and to determine the best frequency and intervals of SDF applications."	All covered by the authors.	Well conducted SR; the search was comprehensive including searching for on-going trials, theses and dissertations. The authors attempted to contact studies' authors to obtain missing information. It referred to *a priori* designed protocol. However, its status in PROSPERO had not been updated and still "ongoing" although it has been completed and published.

Table 3-6 Findings of coronal caries SRs

Systematic review	Included SDF studies			Systematic review authors' stated limitations	Systematic review authors' stated conclusions	Umbrella review authors' additional limitations	Umbrella review authors' comments
	Number of studies sample size (range	Countries of origin (number in each country)	Publication date range				
Rosenblatt (2009) **Silver diamine fluoride: a caries "silver-fluoride bullet"**	2 827 (375-452)	Cuba (1) Hong Kong (1)	2002-2005	"Neither study provided a power calculation. This, therefore, is a limited dataset upon which to build a new preventive strategy." "Only one of the two identified and qualifying study extended their research to permanent teeth. One study only examined only maxillary interior, and not posterior teeth. This limits the data upon which one might base clinical application of SDF."	"SDF can have a significant and substantial benefit in arresting and preventing caries. By implication, SDF could provide a new quantitative preventive benefit for individuals and populations."	No referral to a priori designed protocol. Small number of included studies. The authors did not declare that there was no conflict of interests.	There is limited evidence to support the effectiveness of SDF in preventing/arresting caries because the small number of included studies. Moreover, one study should not have been included because it compared the effectiveness of SDF to water, while the research question is clearly stated:" Will SDF more effectively prevent caries than FV?"
Duangthip (2015) **Non-surgical treatment of dentin caries in preschool children – systematic review**	3 678 (91-375)	China (2) Brazil (1)	2002-2012	"Few studies were included in the review." "Only English papers were reviewed, and this may lead to a reporting bias." "Some included studies were assessed as at moderate or high risk of bias" "Although the inter- and intra-reliability of all included studies in this review were high, a major concern is a lack of an accepted clinical gold standard which can reliably differentiate between active and arrested lesions." "It should be noted that papers of co-authors of this review were finally included and there may be bias."	"There is limited evidence to support the effectiveness of SDF applications once/twice a year and that of daily tooth brushing with fluoride toothpaste in arresting or slowing down the progression of active dentin caries in primary teeth in preschool children. More well-designed RCTs are required to confirm these findings."	No referral to a priori designed protocol.	Only 3 English studies were included (2 at low risk of bias and 1 at a high risk of bias), which limits the evidence regarding the effectiveness of SDF in arresting dentine caries in primary teeth.

Systematic review	Included SDF studies			Systematic review authors' stated limitations	Systematic review authors' stated conclusions	Umbrella review authors' additional limitations	Umbrella review authors' comments
	Number of studies sample size (range	Countries of origin (number in each country)	Publication date range				
Gao (2016a) **Clinical trials of silver diamine fluoride in arresting caries among children: a systematic review**	19 Some trials did not report the sample size	Brazil (5) China (5) Japan (4) Hong Kong (2) Nepal (1) Cuba (1) Argentina (1)	1969-2016	"It is noteworthy that the reliability of some studies included in this review was relatively low because most of the clinical studies on SDF were conducted before the Consolidated Standards of Reporting Trials (CONSORT) statement was developed."	"SDF was commonly used at a high concentration (38%, 44,800 ppm fluoride) and is effective in arresting dentine caries in primary teeth. There is no consensus on its number and frequency of application to arrest caries. Further studies are necessary to develop evidence-based guidelines on its use in children."	No referral to a priori designed protocol. Studies conducted before 2002 were at low quality.	The authors have included the countries' languages where most of SDF studies are likely to have taken place and the search was quite comprehensive in terms of coverage of databases. In conclusion, this SR included 19 studies of different languages and showed that 38% SDF is effective in arresting dentin caries in primary teeth.
Gao (2016b) **Caries remineralisation and arresting effect in children by professionally applied fluoride treatment – a systematic review**	7 2548 (60-976)	China (2) Brazil (2) Hong Kong (1) Cuba (1) Nepal (1)	2001-2012	"There are only a few clinical trials reported in the literature. The five publications selected had different duration, dentition, starting age, mode of delivery, concentration and frequency of SDF treatment." "This review may not be comprehensive because those studies published in Japanese, Chinese, Spanish or Portuguese were not included."	"Silver diamine fluoride solution at 38 % is effective in arresting active dentine caries. Because the number of clinical trials that studied the arresting effect of dental caries is limited, more clinical trials should be performed."	No referral to a priori designed protocol.	Taking into account the several limitations this review has, SDF has been found to be effective in arresting dentine caries based on 6 RCTs. Only one study assessed the effectiveness of SDF in remineralising early enamel caries. Therefore, it was not sufficient to build an evidence.

Systematic review	Included SDF studies			Systematic review authors' stated limitations	Systematic review authors' stated conclusions	Umbrella review authors' additional limitations	Umbrella review authors' comments
	Number of studies sample size (range	Countries of origin (number in each country)	Publication date range				
Contreras (2017) **Effectiveness of silver diamine fluoride in caries prevention and arrest: a systematic literature review**	7 3043 (22-1016)	Brazil (2) Cuba (1) China (1) Philippines (1) Hong Kong (1) Nepal (1)	2005-2016	"The review analysed only manuscripts written in English; however, results of additional SDF clinical trials conducted in countries where SDF is available have been published in other languages. This filter could have introduced bias into the analysis. Moreover, an analysis of bias was not conducted, because the authors were unable to contact the primary authors of the studies and clarify issues related to the risks assessed or adverse events and side effects (publication bias). Trial reporting of the assessed studies could suggest additional biases such as selection (concealment of allocation sequence), detection (failure to blind participants and personnel), and other biases. In addition, differences between examiner criteria or stringency of the examiner limited a comparative analysis of caries arrest detection."	"SDF, at concentrations of 30% and 38%, is more effective than other preventive management strategies for arresting dentinal caries in the primary dentition. Additionally, 30% and 38% concentrations of SDF show potential as a caries preventive treatment in primary teeth and permanent first molars. Standardized SDF protocols must be developed to allow meaningful study comparisons and establish treatment guidelines."	No referral to a priori designed protocol.	The authors did not declare that there was no conflict of interests. This SR has some limitations, but it shows that SDF 30% and 38% is effective in preventing and arresting caries in the primary dentition and permanent first molars.
Chibinski (2017) **Silver Diamine Fluoride Has Efficacy in Controlling Caries Progression in Primary Teeth: a systematic review and Meta-Analysis**	11 4089 (60-1016)	Brazil (3) China (2) Hong Kong (2) Cuba (1) Nepal (1) Philippines (1) Turkey (1)	2002-2016	"The most remarkable feature of the included papers is the great variation of the measured outcomes. The outcomes were: (1) number of inactive carious surface (2) number of active carious surface (3) dmft index (4) number of teeth with inactive carious lesions (5) number of teeth with new carious lesions ;(6) number of inactive carious lesions in the first permanent molars."	"SDF is more effective than other active treatments or placebo for caries arrestment in primary teeth. The body of evidence was of high quality for primary teeth. There is not enough evidence to draw a conclusion about caries arrestment in first permanent molars."	All covered by the authors	Well conducted SR; the authors searched the grey literature, dissertations and thesis, and contacted the authors of some studies for additional details, and it referred to *a priori* designed protocol. However, its status in PROSPERO had not been updated and still "ongoing" although it has been completed and published. This supports the hypothesis that SDF is effective in arresting caries in primary teeth.

Systematic review	Included SDF studies			Systematic review authors' stated limitations	Systematic review authors' stated conclusions	Umbrella review authors' additional limitations	Umbrella review authors' comments
	Number of studies sample size (range	Countries of origin (number in each country)	Publication date range				
Oliveira (2019) **The Effect of Silver Diamine Fluoride in Preventing Caries in the Primary Dentition: a systematic review and Meta-Analysis**	4 1038 (91-452)	Brazil (2) China (1) Cuba (1)	1991-2012	"Although we performed a comprehensive search, we found only a very small number of clinical trials having the development of new caries lesions as outcome measure. Interestingly, the trials identified for this review were primarily designed to investigate the SDF potential for dental caries arrest and most applied SDF to carious lesions only."	"Since SDF topical applications are simple, safe, inexpensive, and have the potential to both arrest and prevent dental caries in primary teeth, they may have a significant impact on reducing the burden of untreated dental disease in children. Nevertheless, the evidence on the preventive effect of SDF is based on only 2 small positive clinical trials with important limitations regarding study design and implementation. More rigorously designed studies, reported according to the Consolidated Standards of Reporting Trials Statement (CONSORT), are warranted to ensure unbiased high-quality evidence on the benefits of SDF applications for caries prevention."	All covered by the authors	Well conducted SR; the search was comprehensive including searching for on-going trials, theses and dissertations. The authors attempted to contact studies' authors to obtain missing information. It referred to *a priori* designed protocol. However, after going back to the registered protocol in PROSPERO, a deviation was noted between the protocol and the actual review, but it was justified after contacting the authors of the SR. Moreover, its status in PROSPERO had not been updated and still "ongoing" although it has been completed and published.

3.4.4.1 Root carious lesions management in adults

For root carious lesions prevention and arrest, all four SRs found the direction of effect favoured SDF i.e. there were more prevented and arrested lesions with the use of SDF when compared to other interventions/ negative controls. Table 3-7 presents the different outcome measures employed in each SR along with their results.

Carious lesions prevention

There were four SRs that looked at root carious lesions prevention (Gluzman et al., 2013, Wierichs and Meyer-Lueckel, 2015, Hendre et al., 2017, Oliveira et al., 2018). The investigators in all studies compared 38% SDF to placebo. However, different outcome measures were employed. One SR (Gluzman et al., 2013) at high risk of bias reported, based on one study, that the success rates were 72% higher for the SDF. The MD for changes in the Decayed, Missing, Filled Root Surfaces index DMFRS/DFRS was − 0.33 (95% CI = − 0.39, − 0.28) for SDF based one high risk of bias SR with meta-analysis of two studies (Wierichs and Meyer-Lueckel, 2015). The PF range was 25–71% for SDF based on one low (Oliveira et al., 2018) and one high risk of bias (Hendre et al., 2017) SRs including four studies.

Carious lesions arrest

There were three SRs looked at root carious lesions arrest (Wierichs and Meyer-Lueckel, 2015, Hendre et al., 2017, Oliveira et al., 2018). The investigators in all studies compared 38% SDF to placebo. However, only one SR that of high risk of bias presented numeric results and reported that the PF was 100 to 725% higher for SDF with data from two studies (Hendre et al., 2017). One low risk of

bias SR reported that SDF was significantly more effective than placebo in arresting root carious lesions (pooled results were not calculated) (Oliveira et al., 2018). Similarly, one high risk of bias SR found that SDF can be efficacious to decrease progression of root carious lesions (no numeric results reported) (Wierichs and Meyer-Lueckel, 2015).

Table 3-7 Outcomes and outcome measures of root caries SRs

Outcome	Systematic review	Outcome measures with results					No. of studies used in synthesising these results*	Summary**
		Success rates	PF	MD	WMD	NNT		
Root caries prevention	**Gluzman, 2013**	72% compared to placebo	_____	_____	_____	_____	1 study	**Success rate** One SR reported success rate for annually applied SDF at 36 months 72%. **MD** One SR measured MD for SDF compared to placebo at (24-36) months intervals, MD= -0.33. **PF** Two SRs compared SDF to placebo at (12-36) months intervals, PF=25-71%.
	Wierichs, 2015	_____	_____	MD= -0.33 (95% CI= -0.39, -0.28) at 24-36 months	_____	_____	2 studies	
	Hendre, 2017	_____	PF= 25% in a 24-month study PF= 71% in a 36-month study	_____	_____	NNT= 3.3 in a 24-month study NNT= 2.5 in a 36-month study	1 study at 24-months follow-up 1 study at 36-months follow-up	
	Oliveira, 2018	_____	PF= 68% (95% CI= 54-83%) at 12 months PF= 50% (95% CI= 37-63%) at 24 months PF= 60% (95% CI= 45-57%) at ≥ 30 months	_____	WMD= -0.48 (95% CI= -0.69 to -0.27) at 12 months WMD= -0.56 (95% CI= -0.77 to -0.36) at 24 months WMD= -0.80 (95% CI= -1.19, to 0.42) at ≥ 30 months	_____	2 studies at 12-months follow-up 3 studies at 24-months follow-up 2 studies at ≥ 30-months follow-up	
Root caries arrest	**Hendre, 2017**	_____	PF was 725% greater than placebo at 24 months PF was 100% greater than placebo at 30 months	_____	_____	NNT= 1.8 in a 30-month study	1 study at 24-months follow-up 1 study at 30-months follow-up	**PF** One SR reported that PF for SDF was (100%-725%) greater than placebo at (24-30) months intervals.

* This might differ from the number of included studies in some systematic reviews because synthesising all included studies' results was not always possible.
** The summary presents various outcomes where meaningful results could be combined
PF: Prevented Fraction, MD: Mean Difference, WMD: Weighted Mean Difference, NNT: Number Need to Treat

3.4.4.2 Coronal carious lesions management in children

For coronal carious lesions prevention and arrest, all seven SRs focused mainly on the primary dentition and all reported that SDF outperformed the comparators regardless of the outcome measure. Table 3-8 presents the different outcome measures employed in each SR along with results.

Carious lesions prevention

Coronal carious lesions prevention was reported in three SRs (Rosenblatt et al., 2009, Contreras et al., 2017, Oliveira et al., 2019). One SR at low risk of bias focused only on the primary dentition (Oliveira et al., 2019), and one SR at unclear (Contreras et al., 2017) and one SR at high (Rosenblatt et al., 2009) risk of bias focused on the primary dentition and first permanent molars. Different concentrations of SDF was compared to placebo, FV or GIC. Two SRs calculated PF along with other different outcome measure. However, one SR presented only studies' original studies.

The PF for 38% SDF compared to placebo ranged from 70 to 78% in the primary dentition based on two SRs (Rosenblatt et al., 2009, Oliveira et al., 2019) including two studies and was 64% in the permanent first molars based on one SR (Rosenblatt et al., 2009) with one study (Llodra et al., 2005). For SDF compared to FV in the primary dentition the PF was 54% based on one SR (Oliveira et al., 2019) with one study (Chu et al., 2002b). The same SR reported that glass ionomer cement was more effective than 30% SDF at 12 months, PF= −6%, but the difference was not statistically significant. One SR presented studies' original results and concluded that SDF showed potential as a caries preventive treatment in the primary dentition and for first permanent molars (Contreras et al., 2017).

Carious lesions arrest

Coronal carious lesions arrest was the outcome looked at the most with six SRs investigating it (Rosenblatt et al., 2009, Duangthip et al., 2015, Gao et al., 2016b, Gao et al., 2016a, Chibinski et al., 2017, Contreras et al., 2017). Three SRs were at low (Gao et al., 2016b, Gao et al., 2016a, Chibinski et al., 2017), one at unclear (Contreras et al., 2017) and two at high (Rosenblatt et al., 2009, Duangthip et al., 2015) risk of bias SRs including eight studies. Three SRs reported the success rate of SDF treatment, while RR or NNT was calculated in in one SR. However, one SR presented only studies' original results.

The reported 38% SDF arrest rates in the primary dentition ranged from 65 to 91% based on three SRs (Duangthip et al., 2015, Gao et al., 2016b, Gao et al., 2016a). These were 38 to 44% for FV, 39 to 82% for GIC, and 34% for placebo. The PF based on one SR (Rosenblatt et al., 2009) with two studies ranged from 55 to 96% in favour of 38% SDF when compared to FV or placebo in primary dentition. However, this was 100% for permanent first molars based on one study (Llodra et al., 2005). The RRs were 1.66 for SDF compared to FV or ART and 2.54 compared with placebo/no treatment based on one SR which focused only on the primary dentition (Chibinski et al., 2017) and including two studies. One SR presented the studies' original results and concluded that SDF at concentrations of 30% and 38% is more effective than other strategies in arresting coronal carious lesions in primary dentition (Contreras et al., 2017).

Table 3-8 Outcomes and outcome measures of coronal caries SRs

Outcome	Systematic review	Outcome measures with results					No. of studies used in synthesising these results*	Summary**
		Success rates	PF	RR	WMD	NNT		
Coronal caries prevention	Rosenblatt, 2009	_____	Lowest PF= 70.3%	_____	_____	Highest NNT 0.9 (95% CI = 0.4- 1.1)	2 studies	**PF** Two SRs compared SDF to placebo at different time intervals, PF=70-78%. GIC was reported to be more effective than SDF at 12 months in one SR, PF= -6%, but the difference was not statistically significant.
	Oliveira, 2019	_____	Placebo: PF = 77.5% (95% CI= 68-78%) at ≥ 24 months FV: PF = 54.0% (95% CI= 27-73%) at ≥ 24 months GIC: PF= –6.09% (95% CI= -36-16%) at 12 months	_____	Placebo: WMD = –1.15 (95% CI= -1.48 to -0.82) at ≥ 24 months FV: WMD = –0.43 (95% CI= -0.70 to -0.16) at ≥ 24 months GIC: WMD= 0.34 (95% CI= -1.02 to 1.70) at 12 months	_____	2 studies comparing SDF to placebo 1 study comparing SDF to FV 1 study comparing SDF to GIC	
Coronal caries arrest	Rosenblatt, 2009	_____	lowest PF 96.1%	_____	_____	Highest NNT 0.8 (95% CI = 0.5-1.0)	2 studies	**Success rates** Four SRs reported success rates. These ranged from SDF: (65-91%); FV: (38-44%); GIC: (39-82%); placebo: 34% at (6-36) months intervals. **PF** One SR reported that the lowest PF for SDF compared to FV and placebo in the included studies was 96.1%. **RR** One SR included 2 studies that compared SDF to FV or ART restorations. (RR=1.66). It included 2 studies that compared SDF to placebo/no treatment (RR=2.54).
	Duangthip, 2015	SDF (65-91%) compared with no treatment (34%), FV (38-44%) and interim GIC (39-82%).	_____	_____	_____	_____	3 Studies	
	Gao, 2016a	86% (95% CI= 47-89%) at 6 months 81% (95% CI= 59-93%) at 12 months 78% (95% CI= 70-85%) at 18 months 65% (95% CI= 35-86%) at 24 months 71% (95% CI= 65-83%) at ≥ 30 months	_____	_____	_____	_____	5 studies at 6-months follow-up 6 studies at 12-months follow-up 4 studies at 18-months follow-up 4 studies at 24-months follow-up 4 studies at ≥ 30-months follow-up	
	Gao, 2016b	66% (95% CI= 41-91%)	_____	_____	_____	_____	5 Studies	
	Chibinski, 2017	_____	_____	Active treatment: RR= 1.(95% CI= 1.41–1.96) Placebo: RR= 2.54 (95 CI=1.67–3.85).	_____	_____	2 studies comparing SDF to active materials 2 studies comparing SDF to placebo	

* This might differ from the number of included studies in some systematic reviews because synthesising all included studies' results was not always possible.
** The summary presents various outcomes where meaningful results could be combined
PF: Prevented Fraction, RR: Risk Ratio, WMD: Weighted Mean Difference, NNT: Number Need to Treat

3.4.5 Adverse events and side effects

Eight SRs reported adverse events and side effects associated with SDF (Rosenblatt et al., 2009, Duangthip et al., 2015, Gao et al., 2016b, Gao et al., 2016a, Contreras et al., 2017, Hendre et al., 2017, Oliveira et al., 2018, Oliveira et al., 2019). The most commonly reported adverse event was black staining of the arrested carious lesions. However, older adults rarely complained about this. Similarly, the discolouration was acceptable in children, causing concern for only 7% of participants in one study (Chu et al., 2002a) . Moreover, one SR (Oliveira et al., 2019) described the parental satisfaction with children's dental appearance at 24-month follow up was similar between experimental and control groups. One SR (Rosenblatt et al., 2009) reported that SDF caused 24-hour tissue sensitivity in three of the 153 participants in one study (Chu et al., 2002a) .

Reversible, small, mildly painful white lesions in oral mucosa, due to inadvertent contact with SDF, were reported; these healed uneventfully within 48 hours. There was no difference in pulpal irritation incidence between the control and experimental groups. Other postulated adverse events, such as metallic taste or burning sensation were not reported in any of the studies. No serious adverse events, such as allergic reactions or, acute or chronic toxicity were reported.

3.5 Discussion

Eleven SRs (of 30 studies) investigating SDF for caries prevention and/or arrest were identified; seven focused on coronal caries in children, and four on root caries in adults. It is notable that there were so many SRs compared to the number of primary studies in this research field. The high ratio of studies to SRs, with several published after 2015, could indicate that no single SR seems to have incorporated all the evidence and comprehensively covered the topic. This umbrella review has attempted to address this by systematically appraising the evidence from the SRs using a transparent methodology. It found that all SRs, despite variability in methodology, reported SDF to be effective for caries prevention and arrest of carious lesions.

Interpretation of the results of umbrella reviews does not include scrutiny of the individual studies that are included in the SRs. Therefore, the conclusions rely on the interpretation of the SRs' authors. This is in line with the accepted umbrella review methodology and capitalises on the fact that the original studies should have had their qualities appraised within the SR in which they were reported.

With 11 SRs including 30 studies, the overlap in studies across SRs was very high in both matrices. Consequently, repeated primary studies would have had unintentionally stronger weighting in any meta-analyses had this been undertaken. This, together with heterogeneity of comparators and outcome measures limited synthesis of the results and precluded meta-analyses. In addition, each meta-analysis was not re-calculated to confirm validity. However, allowing for these caveats, this umbrella review is the first such review systematically summarising the current evidence for the effectiveness of SDF for caries prevention and arrest. It followed a systematic approach that included a

comprehensive search strategy of five databases with independent, duplicate SR selection and data extraction and an accepted method to assess risk of bias.

Multiple SDF studies have been set in non-English speaking countries such as China and Brazil. Thirteen out of the 30 unique primary studies were published in non-English languages. However, five SRs excluded non-English studies, and this is likely to have introduced bias into their dataset, analyses and conclusions.

There was wide variability in the number of included studies ranging from only two (Rosenblatt et al., 2009) up to 19 (Gao et al., 2016b) even when they investigated similar interventions/comparators, aims and outcomes as well as including similar study designs. Without further investigation, it was not possible to determine the reason for this, however there is an interesting difference between the coronal and root caries SRs. In the root caries SRs, (Figure 3-4) shows that the more recently the SR was carried out, the more primary studies were included. This contrasts with the irregular pattern of study inclusion seen for the coronal caries SRs

Figure 3-5). This pattern is not explained by the search timeframe or year of publication as more recent SRs would be expected to include more recently published studies in addition to capturing all previous ones. Although it was not within the remit of this review to undertake a full exploration of the reasons for inclusion and exclusion of studies in the SRs, it does not seem to be explained by differing inclusion and exclusion criteria, or other methodological decisions. Some of these findings might offer insight into this and inform future work looking at the quality of SRs.

To highlight some examples of the differences in included primary studies, one primary study investigated the effectiveness of Nano Silver Fluoride (NSF) for preventing and arresting carious lesions in children (dos Santos Jr et al., 2014). It was included in a SR investigating SDF (Chibinski et al., 2017) and the justification given, on contacting the authors, was because NSF contained the same components as SDF; this effect remained the same even when silver fluoride was chemically treated to obtain nanoparticles of silver. However, other SRs excluded this study, possibly because the authors viewed NSF as different from SDF. Alternatively, they did not detect this paper in their search. On the other hand, the same SR (Chibinski et al., 2017) excluded a study investigating SDF in arresting occlusal carious lesions in first permanent molars (Braga et al., 2009) because the method of evaluation was based on qualitative scores. However, it was included in three other SRs (Gao et al., 2016b, Gao et al., 2016a, Contreras et al., 2017). Although this finding is incidental and was not one of the aims of the umbrella review, it is notable and perhaps worth investigating further. It is not possible to quantify this in terms of quality of the individual SRs and this is perhaps a limitation of umbrella reviews.

The usefulness of the risk of bias scoring tools is also questioned with these findings. If one of these SRs was assessed individually, it could score at low risk of bias and be considered as a good SR for basing policy on, yet there could be many primary studies not included and a resulting hidden high risk of bias with no insight into the consequences of omitting certain studies. Poor decisions to include or exclude studies could easily go undetected. The lack of comprehensiveness in the SRs is not fully related to low quality and only revealed by comparing the SRs.

These findings highlight the need for meticulous attention to be paid during the primary study selection processes and for those appraising SRs to be aware that this might be a shortcoming not detected during quality appraisal. It also stresses the need for SRs to provide data justifying the exclusion of each primary study, and not simply report the total number of excluded studies with overall reasons. This would help clarify whether all possible studies were found through searching and rule out selection bias. So, even SRs at low risk of bias, according to ROBIS tool, might fail to provide healthcare decision makers with accurate evidence depending on how they include or exclude studies relevant to their question.

For SDF, all the SRs pointed to evidence of a positive effect rather than conflicting results depending on which SR was looked at. For the root caries SRs, the main limitation was around conclusions being based on a limited number of included studies (one SR drew conclusion based on only one study). This raises the need for more well-conducted RCTs investigating SDF for root carious lesions management. Imposing language restrictions and the absence of *a priori* designed protocol affected the risk of bias in three out of the four SRs. One SR, in the conclusion, supported the use of SDF for treating dentine hypersensitivity even though this was neither included in the search nor discussed through the SR (Hendre et al., 2017).

For the coronal caries SRs, a larger number of studies was included in the SRs. However, the quality of included studies varied, with those conducted before 2002 being of low reliability. In addition, the methodology and the outcome measurements for caries varied between included studies which made combining the results challenging. This highlights the need for designing a standardised methodology and following a core outcome set (Williamson et al., 2017), if

possible, for studies in reporting their results, in order to enable SRs to synthesis the evidence from all available relevant studies. See Table 3-5 and Table 3-6 for further details about the limitations of each included SR.

Another finding worth noting was that the search in the PROSPERO register retrieved six ongoing, apparently unfinished SRs. Three were completed and published however their authors did not seem to have update these records in PROSPERO (Chibinski et al., 2017, Oliveira et al., 2018, Oliveira et al., 2019).

Overall, all SRs reported that SDF was effective in managing caries. However, earlier ones tended to overstate conclusions around SDF's effectiveness given the limited number of trials they were based on, and the SRs' high risk of bias. More recent SRs reported increasing numbers of trials and were of lower risk of bias.

For root caries *prevention and arrest*, the SRs were based on only four clinical trials. However, all sudies were assessed as high quality in the SRs. There was a large variability in the number of studies included in the coronal caries SRs and the reasons for this were unclear. For coronal caries *prevention*, it is noteworthy that the number and quality of studies included in the SRs was low which questions the evidence base around SDF for coronal caries prevention. For coronal caries *arrest*, an increased number of SRs have reported stronger evidence to support SDF use in the primary dentition. There is insufficient evidence to draw conclusions for its use in permanent teeth in children as there are so few studies.

3.6 Update

A more recent search following the same search strategy used before was conducted to retrieve any SRs concerned with SDF published after the date of the original search (July 2018 – June 2020) in PubMed. This is to identify any conflicting findings from the findings in the included SRs in the Umbrella review.

Interestingly, eight SRs concerned with SDF were published within this period (Subbiah and Gopinathan, 2018, Slayton et al., 2018, Tedesco et al., 2018, Trieu et al., 2019, Urquhart et al., 2019, Meyer-Lueckel et al., 2019, Schmoeckel et al., 2020, Zhang et al., 2020). This relatively high number of SRs of SDF published within the last two years reflects the increased interest in SDF. However, only three unique RCTs (Fung et al., 2016, Duangthip et al., 2018b, Fung et al., 2018) were not included in the SRs included in the umbrella review and appeared in those new eight SRs.

The findings of these SRs, however, echo the findings of the previous SRs included in this umbrella review and supported the use of SDF for managing carious lesions in children and adults.

3.7 Conclusions

Although there are not many studies, there is a consistent and progressively strengthening body of research that supports SDF's effectiveness for arresting coronal carious lesions in children in the primary dentition and arresting and prevention root carious lesions in older adults.

However, the limited number and questionable quality of studies investigating SDF for preventing coronal carious lesions in children, questions the evidence base around its use in such cases. Similarly, there are too few studies and insufficient evidence to draw conclusions on the use of SDF in permanent teeth in children.

The next chapter will explore DPs perspectives, on treatment options for the management of dental carious lesions in children, with a focus on SDF.

3.8 Summary

Eleven SRs were included in the umbrella review; four focussing on SDF for root caries in adults and seven on coronal caries in children. These cited 30 studies (4 root caries; 26 coronal caries) appearing 63 times. Eight systematic reviews reported adverse events.

Using the ROBIS tool, five SRs were of "low", one "unclear" and five "high" risk of bias. A citation matrix was generated and the CCA was calculated separately for root and coronal caries SRs. The overlap of studies across SRs was very high in each matrix.

No serious adverse events, such as allergic reactions or, acute or chronic toxicity were reported in the SRs. The most commonly reported adverse event was black staining of the arrested carious lesions. Reversible, small, mildly painful white lesions in oral mucosa, due to inadvertent contact with SDF, were reported.

For root caries prevention and arrest, the SRs were based on only four clinical trials. However, all studies were assessed as high quality in the SRs.

For coronal caries prevention, the number and quality of studies included in the SRs was low which questions the evidence base around SDF for coronal caries prevention. For coronal caries arrest, an increased number of SRs have reported stronger evidence to support SDF use in the primary dentition.

CHAPTER FOUR: DENTAL PROFESSIONALS' VIEWS OF SILVER DIAMINE FLUORIDE FOR THE MANAGEMENT OF CARIOUS LESIONS IN CHILDREN: A QUALITATIVE STUDY

4.1 Introduction

This chapter focuses on a second element of EBP; clinical expertise and expert opinions (Figure 4-1) (Sackett et al., 1996). Having established, in the previous chapter, the evidence base around the use of SDF for managing carious lesions in children, and concluding that SDF can be effective in managing carious lesions in primary teeth, this chapter will explore DP's clinical experience and preferences towards using SDF to manage carious lesions in primary dentition.

Figure 4-1 Clinical expertise component of EBP

In order to explore dental professionals' clinical skills and past experience, through their attitudes, opinions, views and preferences (Straus et al., 2018), a qualitative approach was undertaken. Qualitative research is mainly exploratory in nature and involves the researcher collecting, analysing and interpreting data to gain a better understanding of a problem. Through this process, ideas and hypotheses may be formulate (Ma, 2000).

Unlike, quantitative research, in which the researchers collect data to empirically test preconceived theories or hypotheses, researchers carrying out qualitative research often utilise an inductive approach by firstly collecting data and then deriving explanations from that data (Silverman, 2016). Qualitative data is generally unstructured, unmeasurable and descriptive in nature rather than numerical. When carrying out qualitative research, the researcher follows a flexible structure allowing them to collect additional data on the basis of the initial

data collected i.e. the researcher can adapt the research process in accordance with emerging results (Pope et al., 2000).

Interviews are a qualitative approach that can provide a deeper understanding of a particular social phenomenon being investigated and are considered suitable where little is already known or understood about the topic under review or where comprehensive perceptions are needed from individual participants (Gill et al., 2008). Interview study designs can vary depending on the amount of latitude given to interviewees to discuss their views and experiences: unstructured, semi-structured and structured. Adopting a particular design depends on several considerations including: the phenomena in question, characteristics of the sample, and available time and resources (Corbin and Strauss, 2014). In the work being conducted here, since this part of the study was exploratory in nature, participants' elaborations on the relevant topics were needed (Frankel and Devers, 2000). Therefore, semi-structured, in depth interviews, which tend to be conversational in nature were deemed the most appropriate approach. This involved using a series of related questions to understand the interviewee's views and perceptions (Serry and Liamputtong, 2013).

Limited research has been carried out around the preferences of DPs i.e. dentists, dental therapists, dental hygienists or dental nurses for different treatment options for managing dental caries in the primary dentition in children. In particular, there is limited evidence about the preferences of DPs, in relation to the use of SDF. In addition, it appears that the uptake of SDF in the UK remains limited unlike other Western countries (Timms et al., 2020). Therefore, this was an area ripe for exploration.

A concise version of this qualitative exploration of DPs acceptability of SDF has been published at the BMC Oral Health Journal (**Publication 4**).

4.2 Aim and objectives

The aim of this phase of the PhD was to explore DPs' views regarding treatment options to manage dental carious lesions in the primary dentition, with a focus on SDF.

The specific objectives were to explore DPs':

1. existing knowledge, and experience of SDF;
2. perceptions of the advantages and disadvantages of SDF;
3. opinions on the key barriers and enablers to the use of SDF for the management of carious lesions in primary dentition; and
4. views regarding children's and parents/carers' acceptability of SDF.

4.3 Methodology

4.3.1 Study design

Semi-structured telephone or face-to-face audio recorded interviews with a range of DPs (**Appendix *5***).

4.3.2 Ethical considerations

This study was approved by University of Dundee Schools of Nursing, Health Sciences and Dentistry Research Ethics Committee (application number: 2018012_Seifo). The study was approved by the Research and Development Managements at NHS Tayside and NHS Grampian (IRAS ID: 252305) (**Appendix *6***).

4.3.3 Setting and participants

DPs comprising dentists, dental therapists, dental hygienists and dental nurses from NHS Tayside and Grampian in Scotland were invited to participate. The interviews took place between December 2018 and June 2019.

4.3.4 Recruitment

In order to ensure the diversity of the study population, a purposive sampling strategy was adopted. This is a non-random way of sampling, to ensure that the sample represents a range of DPs with different backgrounds and varying experiences (Robinson, 2014).

A purposive sample of DPs was recruited through Dundee Dental School and Hospital (who had a focus on children), General Dental Practices, the SDPBRN's database of REPs, VDPs, in the East and North East Regions' training schemes and NHS Grampian and Tayside Public Dental Services.

Potential participants were sent an invitation pack containing a participant information sheet (**Appendix *7***), a reply slip (**Appendix *8***) and a freepost envelope. Participants had the option to return the reply slip in the freepost envelope provided or contact the researcher directly by telephone or email.

Interview dates were arranged at times convenient to the participant. Prior to the interview, participants were given the opportunity to ask any questions and confirm they were happy to take part, and consent was explained and obtained. For face-to-face interviews, the consent process was carried out in person, while for over-the-phone interviews consent was discussed and then agreement to participate (if given) was audio recorded before the audio-recorded telephone interview (**Appendix *9***).

4.3.5 Withdrawal procedure

Participants had the right to withdraw at any stage in the study without providing a reason.

4.3.6 Data collection

Semi-structured telephone or face-to-face interviews were conducted by the researcher in a suitable venue. Open-ended questions and probing were used.

An interview topic guide was developed to explore, from DPs' perspectives, the acceptability of, and barriers and enablers to the use of, SDF and their perceptions of children's and parent/carers' preferences. The topic guide was informed by the available information about the advantages, disadvantages, uses and indications of SDF reported in the literature. Areas of discussion focused on four categories 1) DPs' experience with children, 2) DPs' experience and knowledge of SDF, 3) DPs' perceptions of using SDF in practice, and 4) DPs' perceptions of parents perceived attitude toward their child dental treatment.

The topic guide (**Appendix *10***) was piloted with two DPs to ensure the questions were clear to the target population. Data from pilot interviews were not included in the analysis. A small number of questions were re-worded as a result of the pilot interviews findings. The topic guide was developed to direct interaction whilst giving the participants the opportunity to report their own thoughts, feelings and other related areas in more details. If the participant provided brief responses, the interviewer then used cues and prompts to encourage the interviewee to elaborate on their response or consider other aspects of the question further (Adams, 2015).

It was not possible to specify the number of participants required to draw compelling meaning from the results before commencing the interviews. It is generally agreed that there is no ideal number of interviews needed to attain valid interpretations from the data, and it is dependent on the breadth of the interview topic and diversity of details yielded from the interviewees (Patton, 2014). Therefore, Interviews continued until data saturation was achieved i.e. when no new themes, categories or explanations were emerging from the data, using a stopping criterion of three to ensure data saturation (Francis et al., 2010).

4.3.7 Data analysis

Thematic analysis was undertaken using the framework approach as a broad guide to organise and classify data according to key issues, concepts and emerging themes. (Ritchie and Spencer, 2002). All interviews were recorded and transcribed verbatim. The researcher transcribed two interviews and the rest were transferred to a transcription service. However, all identifiable data were anonymised before being transferred to the transcription service.

Data management was facilitated by NVivo 12 software, a qualitative data management software programme (QSR International Pty Ltd., Melbourne, Australia). To minimise bias in data analysis, a sample of two interview transcripts were double coded independently by the researcher and one of the PhD supervisors (HC), with experience in qualitative research, and codes were compared to check consistency. The Consolidated Criteria for Reporting Qualitative Research (COREQ) was followed to guide reporting of the data (Tong et al., 2007).

The five stages of data analysis following the framework approach were as follows:(Ritchie and Spencer, 2002);

1- **Familiarisation:** This involves the researcher re-listening to all interview recordings and reading through the transcripts and any notes taken at the time of the interviews. This provides the researcher with an opportunity to articulate and note down initial thoughts and themes.
2- **Identifying a thematic framework:** During this process, the researcher draws upon *a priori* issues and, therefore, the initial framework is often largely descriptive and rooted within these a priori issues.
3- **Indexing:** This is where the data is applied to framework headings and involves identifying sections of the text that are associated with these. This process informs the development of sub-themes. It may be that sections of the text are aligned to two or more themes and when new sub-themes emerge, the researcher will revisit previous transcripts to establish if they are common themes. This process ensures saturation of themes.
4- **Charting:** This involves applying the data from the individual transcripts to the index, this information is then extracted from its original context and rearranged according to the key themes emerging from the data as a whole. This allows comparisons to be made across participants.
5- **Mapping and interpretation:** The final stage aims to draw together the key characteristics of the data and interpret it as a whole. This involves comparing and contrasting experiences and perceptions and explore similarities and differences across the data to provide explanations.

A coding framework was developed following the initial review of three transcripts. This was then assessed by one of the PhD supervisors, HC who was not involved in conducting the interviews. Development of the codebook was an iterative process with adaptations made through discussion as appropriate.

4.4 Results

Fifteen interviews (13 face-to-face interviews and two telephone interviews) with 14 participants between December 2018 and June 2019 were conducted; a short update interview with one participant was conducted after they had applied SDF for the first time. No one withdrew from the study.

Of the 14 participants, 64% (n=9) were female. The clinical experience of participants varied from less than 10 years (n=5), 10-20 years (n=6) and over 30 years (n=3). Of the 14 DPs, 12 were dentists (nine general dental practitioners, one consultant, one core trainee and one vocational trainee, one dental therapist and one dental nurse. Twelve participants were recruited from NHS Tayside and two through NHS Grampian. Table 4-1 summarises the characteristics of participants.

Most interviews lasted, on average 25 minutes in duration and ranged from 10 to 35 minutes with the total interview time being 263 minutes. A few of the interviews were shorter when participants did not have much to discuss i.e. had not had considerable knowledge, or experience with SDF.

Table 4-1 Characteristics of interviewed DPs

Professional role		Health care service		NHS Site		Years of experience		Gender	
Dentist	12	Primary care	6	NHS Tayside	12	Less than 10 years	5	Female	9
Dental therapist	1	Secondary care	8	NHS Grampian	2	10-20 year	6	Male	5
Dental nurse	1					Over 30 years	3		

Three themes emerged from the interviews. These were experience with children, perceptions of using SDF in practice and perceptions of parents'/children's treatment preferences with several subthemes categorised in the latter two themes.

4.4.1 Experience with children

DPs' experience with children varied across the sample depending on the average number of the child patients seen per day in practice from one child to 15-20 children a day. A range of participants agreed that treating children was something they enjoyed doing most of the time. One dentist who reported seeing around seven child patients a day commented:

"It can be quite an uplift to treat a child. You know? It's a little bit of a break in the day from being, you know, serious with adults"

DP 12 (Dentist)

Other participants disagreed with this view, saying that despite having been practicing dentistry for over 30 years, they still felt anxious about providing dental

treatment to children. They emphasised this point by reporting that they would avoid seeing children and would usually refer them directly to the dental therapist or to a female dentist:

"I just find it sometimes quite stressful to treat children and I think female dentists are better. That's rather sexist, but I think, I think women are generally better with kids, and I prefer not to"

DP 14 (Dentist)

It was also reported that newly qualified DPs who did not have much experience with child patients could feel nervous about treating child patients. Accumulating future experience according to them would help build their self-confidence:

"But I think there's always an element of anxiety possibly, because I don't have a terrible amount of experience treating children, I have more experience treating adults obviously, but not so much children so there's always that feeling of what's going to happen?"

DP 10 (Vocational Trainee)

This point was reinforced by other participants who had been practicing for several years. They believed that their accumulated experience with child patients had improved the ways in which they approach children and deliver treatments, resulting in increased confidence:

"Um, and I think with time you, you learn, you learn how to, not only how to deliver the treatment competently, but also how to, how to describe it and how to make, how to make parents and children understand that it really is the best treatment option that we often have……..so I suppose that experience has made me much more confidence to sort of sell the treatment if you like"

DP 2 (Dentist)

A number of participants reported that getting anxious or nervous children through the appointment and gaining their trust and cooperation for future visits was one the most rewarding aspects of paediatric dentistry:

"Sure, my favourite aspect. I say that I'm nervous seeing kids, but when you have a kid where you can make a difference and they actually come up smiling or they start crying, they're like, they're happy at the end, that is really fulfilling to me"

DP 10 (Vocational trainee).

Seeing uncooperative children and working with them to accept treatment was also viewed as one of the most challenging aspects of paediatric dentistry, requiring considerable experience:

"Er, the most challenging part is probably very young children who are pre cooperative or children who are very, very anxious and are non-accepting of treatments under local anaesthetic"

DP 9 (Dentist)

Another challenge, identified by some participants was educating parents to encourage good child oral health They suggested that the child's oral health was not only the DP's responsibility, and not only the child's, but also the whole family's responsibility. These participants suggested that not all parents necessarily feel that they are responsible for their child's oral health:

"Oooh, the most challenging part is I suppose it's educating parents and keeping parents on board to work with you, so that you can actually get those changes and you can … you know, because if you don't have the support at home, then the child often is blamed for the decay and really, it's the parents responsibility. So, it's getting the parent on board in the right way"

DP 11 (Dentist)

It was reported that DPs often see child patients who are afraid of dental treatment even though they had not been to the dentist before. DPs attributed this to children inheriting these fears from their social environment. Therefore, it was suggested that educating parents may be helpful in eliminating these fears:

"Um, usually having to get the parents on board as well um, because I often find that the majority of children have the fear that they've inherited from their parents or siblings or school friends or something like that, rather than they've actually got a definite fear themselves, um, you know, particularly if they've never had things done"

DP 8 (Dentist)

To overcome these challenges, it was suggested that enhanced communication, where treatments are carefully explained to the children and establishing a good relationship with the child, in order to gain their trust and cooperation, may facilitate behaviour change:

"So, I tend to use whatever communication skills work for that particular child. So, I might try four or five different communication approaches, and then whichever one I have that (finger snapping) clicks with the child is the one I'll use"

DP 7 (Dentist)

Another strategy that DPs reported being useful in facilitating cooperation was planning the treatment in a way that would make the child tolerate the treatment gradually, i.e. starting with the easiest procedure that would not expose the child to any pain or discomfort and leaving the most difficult procedure to the end:

“um, I’d try to tailor the treatment such that we built up to the most difficult thing if that were possible. So, say they needed an extraction, I wouldn’t do that first unless, you know, I was absolutely forced to. I would try and do things, so they got to know me”

DP 1 (Dentist)

4.4.2 Perceptions of using SDF in practice

Seven subthemes emerged under this them. These were Knowledge and experience of SDF, perceived advantages of SDF, perceived disadvantages of SDF, perceived barriers for SDF use in practice, perceived enablers for SDF use in practice, perceived uses of SDF and SDF compared to Hall Technique.

4.4.2.1 Knowledge and experience of SDF

A range of DPs interviewed had some knowledge of SDF and several reported having used it in practice. However, DPs were able to articulate that SDF can be used for preventing and arresting carious lesions in children and treating dentine hypersensitivity. The black staining of arrested carious lesions was raised by a range of participants when they were asked what they knew about SDF, with one commenting:

“Um, so I know that it’s a method for arresting carious lesions, uh, and quite like with stainless steel crowns, it has a similar challenge, sometimes, to present to the parents that it’s not going to be very aesthetic because it’s going to stain them black”

DP 12 (Dentist)

A number participants had applied SDF before participating in these interviews. One dental therapist had not applied SDF at the time of their initial interview, however, had a patient booked in for SDF application. A second interview was therefore conducted after they had applied it to gather feedback and explore their initial thoughts and experiences of undertaking the treatment.

"Um, I was worried about doing it beforehand because I've never done it before, but it wasn't as bad as what I thought it was going to be"

DP 5 (Dental therapist)

All participants who had applied SDF before, were employees of Dundee Dental Hospital and School. Overall, participants did not have significant experience applying SDF but demonstrated an interest in doing so in the future. One dentist who had not applied SDF commented:

"I have actually not used it. Erm, I'm presently waiting to get an opportunity"

DP 8 (Dentist)

DPs who had applied SDF, thought the application process was simple and quick. In addition. They reported that in their experience neither parents nor children were concerned about the discolouration associated with SDF:

"Well I must say I've not, I've not encountered any resistance to it from any parent or any child yet. I've, I've not used it on hundreds of children, but I've, I've probably used it on 10 or 15 children now down on the clinic"

DP 2 (Dentist)

4.4.2.2 Perceived advantages of SDF

The perceived advantages of using SDF when compared to other treatment options were explored. It was reported the main advantage of SDF to be the lower levels of cooperation required and as a result the benefit this may have for children who find receiving dental treatment difficult, or patients with special needs or phobias.

"I think it'll be good for patients who we've got very little cooperation …….. So I think the children who have got developmental issues or erm, a low tolerance for dental treatment will be very good because there'll be limited time where they're in the chair"

DP 3 (Dental nurse)

It was highlighted that a certain amount of cooperation would still be required, due to the potential of staining to the skin, face and almost anything it gets in contact with.

"No, I think my only other concern is, um, one of the patient groups that you could use it with are the less cooperative children and my worry with SDF is if they do wriggle and you get it on the skin, it makes a mark. And, actually, therefore actually you need a level of cooperation so that, you know, you don't get it on the skin. And that concerns me"

DP 4 (Dentist)

It was suggested that because SDF requires lower levels of cooperation from the child, this may result in reduced referrals to Secondary Care.

"Oh, I'll give it a go but, uh, I'll often end up referring them to secondary care"

DP 12 (Dentist)

A range of DPs reported that they believe SDF to be a simple, easy and non-invasive approach for managing carious lesions in children because there is no requirement for local anaesthetic, drilling or even excavating carious tissues.

"I think that from the dentist's point of view, I think it's, it's very easy, it's very easy to do, it's um, it doesn't require us to do anything that a child will, will find particularly traumatic at all, erm, so obviously there's no drilling required, there's no local anaesthetic required. Erm, it's really no more difficult than putting on fluoride varnish"

DP 2 (Dentist)

It was however highlighted that the fact that SDF does not require an injection is not necessarily a unique advantage to SDF as there are other treatment approaches used in children's dentistry that also do not require a local anaesthetic, such as crowns fitted using the Hall Technique (HT):

"Well, often we aren't doing injections because we're regularly using Hall crowns. So, that wouldn't be something that I would necessarily, er, be putting forward as a positive thing"

DP 4 (Dentist)

It was also suggested that because the application of SDF is pain free and minimally invasive, it may help to acclimatise children to having dental treatment, i.e. this would help the child to be more aware of the dental environment, and more accepting of more complex dental procedures in future visits. It may also help build a cooperative non dental-phobic patient through their adult life:

"it allows children who perhaps wouldn't be able to tolerate a crown placement or a conventional approach, I think it allows them to, to receive treatment, which

may have to acclimatise them to the dental environment, it might give them a few experiences where they think, "Actually that was easy, that was fine""

DP 2 (Dentist)

"Yeah, a lot of parents, obviously they don't want to see their child going through more invasive work than they need to, you don't want to create dental phobias that last a lifetime either. I think a lot of them would see it as a positive move"

DP 6 (Dentist)

4.4.2.3 Perceived disadvantages of SDF

The perceived disadvantages of using SDF were explored. The issue of aesthetics and the black staining caused by the application of SDF was believed by those interviewed as being the main disadvantage associated with SDF. A range of DPs were concerned with the aesthetic outcome of SDF treatment. They suggested that the permanent discolouration of arrested carious lesions is the biggest disadvantage associated with SDF and could potentially be a barrier to parents' acceptability of its use. One dentist commented:

"Um, I would say the biggest disadvantage with something like silver diamine fluoride would be that get-getting patients to accept it, the fact that it might… they've maybe got lesions that are just pale brown or you know, not very highly coloured, when you paint this on it'll actually turn them black so it'll look quite unsightly"

DP 8 (Dentist)

SDF can also stain the oral mucosa, skin and the clinic surface if contact is made. Therefore, DPs highlighted that meticulous attention is required while applying SDF to avoid any inadvertent spillage or contact.

“So the disadvantages, um, I know that it can stain the mucosa so you need a good, cooperative patient. You also need to be very careful with placing it”

DP 9 (Dentist)

Riva star, which is the commercial SDF product available in the UK is a clear solution. It was reported that the product is inconvenient to use, because it was difficult to notice any accidental spillage before staining occurs:

“I think the disadvantages is that the liquid is clear so you can’t actually see until it’s too late”

DP 5 (Dental therapist)

Another disadvantage reported was the unpleasant taste or sensation associated with SDF:

“I've heard, some patients say like there’s a little fizzing or stinging sensation when it’s being applied. I don’t know if that’s with everyone or just with a small group of patients”

DP 9 (Dentist)

In addition, it was highlighted that it was not easy to access interdental lesions in posterior teeth unless the lesion was fully cavitated and that food packing in the area might obstruct SDF from reaching to the whole carious lesion.

“However, I think that particularly interdental lesions in posterior teeth you have more of an issue with possibly, um, a) getting the silver diamine fluoride to the right area unless it’s completely cavitated and, b) there is an issue, um, with whether you’ve got food packing”

DP 4 (Dentist)

Furthermore, it was highlighted that the size of the micro-brush provided with the SDF kit was not appropriate for interdental lesions in posterior teeth and so reaching these areas was even more difficult:

"and also, um, struggled with approximal lesions, I found that quite difficult because the micro-brush is actually quite large, it's almost that we could use a smaller size micro-brush"

DP 5 (Dental therapist)

4.4.2.4 Perceived barriers for SDF use in practice

In this section DPs' beliefs around the barriers to implementing SDF in practice are presented. These were considered at both the DP level and the child/parent level.

A number of participants suggested that the lack of information and training available about the use of SDF was an initial barrier to using it in practice. One dentist commented:

"*Um, personally I think the lack of knowledge for one. Not having that much exposure means that people won't really use it, that you don't share a lot about it, there's not much advertising about it either*"

DP 10 (Vocational trainee)

This was less of an issue for DPs working within Dundee Dental School who reported receiving exposure and adequate training for new treatment approaches. One dentist commented:

"I mean, obviously, I work in a teaching hospital so I get exposed to new techniques and things, but people in practice, unless they go on courses to learn

how to use it, if they weren't trained with it, they might be very reluctant to use it not knowing anything about it"

DP 1 (Dentist)

It was suggested that introducing a new fluoride agent into practice may be challenging due to FV having been used in practice for a significant period:

"also getting that introduced to practice and changing the culture of the practice, that you should use that instead of fluoride varnish, which is something we've used for a long time, is also a barrier I feel"

DP 10 (Vocational trainee)

Moreover, since SDF is licenced for treating dentine hypersensitivity, this means its use for arresting carious lesions would be considered "off-label" use. This was considered a barrier especially in primary care where DPs get inspected regularly and may have concerns about using a product "off-label".

"The off licence to me is more of an issue if you're trying to get it used in general practice because personally, I would feel less comfortable. Doesn't mean I wouldn't use it, it just means that I would be a bit more cautious in how I'd approach the children"

DP 3 (Dentist)

"what would be interesting to know is indemnity organisations such as Dental Protection, in the event that we were to get sued following use of Silver Diamine Fluoride, would they support us? Or would they say, "You're liable because you've intentionally used an off licence medication for an incorrect purpose". I don't know the answer to that question, but if I was in practice, I would want to know the answer to it"

DP 3 (Dentist)

Contrary to this, it was suggested this would not be an issue as patients have trust in the oral health care provided and are assured that only effective and safe products would be used.

"Yeah, I think that's a minor point. I mean a lot of people in this country certainly if you're coming in here for treatment, they trust that you would only give them products that would be safe and for their intended use and they don't really know what you mean by off licence I guess"

DP 4 (Dentist)

DPs working within NHS Primary care reported that an additional barrier is that SDF is not currently listed in the Statement of Dental Remunerations (SDR). As a result, DPs in NHS primary care practices are not able to claim financially for it. One dentist commented:

"For me, there's gonna be no SDR fee so I'm not gonna be able to claim for using it"

DP 12 (Dentist)

4.4.2.5 Perceived enablers for SDF use in practice

As well as capturing the potential barriers to using SDF in practice, enablers from DPs' perspectives were also explored. DPs suggested that a lack of training around the application of SDF may be one barrier and that therefore, training courses or availability of Continuing Professional Development (CPD) events could be beneficial in encouraging DPs to use it in practice:

"*Having, you know, sort of, adequate training for applying it"*

DP 12 (Dentist)

Moreover, educating DPs about what “off-label” use means and the acceptability of using a product “off-label” may mitigate fears and encourage use.

“I think there needs to be some education of dentists about what off label actually means. They need to be aware when they can use off label products”

DP 1 (Dentist)

“Um, so I think for me it was a barrier initially. Um, but then the more I read about it I realised that being used off licence is okay …… Um, so I'm very happy to do it now”

DP 1 (Dentist)

It was suggested that in order to facilitate the introduction of SDF to parents an information sheet in the practice explaining the advantages, disadvantages and expected outcomes with photos demonstrating arrested carious lesions may also be beneficial.

“It would be good to have some information leaflets, you know something official for the parents to read as well because to them, it’s looking like, “Oh, well, we’re moving away from putting a lovely white filling in a tooth to making it look terrible. Is this actually what we should be doing?” You know? It would be nice to have something official in place that they could read as well, that’s probably a good consideration”

DP 12 (Dentist)

I was suggested that greater evidence about the use of SDF for arresting carious lesions in children may also increase uptake.

“What would encourage me is um, an established um (silence), evidence based err, results”

DP 7 (Dentist)

Furthermore, it was suggested that the introduction of SDF into the SDR may facilitate its use in NHS primary care practices by providing practitioners will the opportunity to claim for it as a treatment option.

"You know, the reality is we're working in an NHS practice and it's, uh, beneficial, of course, that we get remunerated for the child's smile, for getting fluoride applied to the teeth, you know, is that going to be something that they can introduce into the SDR? That would be an important thing, practically"

DP 12 (Dentist)

DPs thought that since the discolouration associated with SDF is the main barrier, any means of minimising the staining impact would be beneficial.

"Um, with regard to being able to use it on a clinical setting um, if there was a way of restricting the discolouration of the teeth or other tissues then that would be a benefit um"

DP 8 (Dentist)

4.4.2.6 Perceived uses of SDF

Cases where SDF could be particularly beneficial were explored from the DPs' perspective. The main advantage identified was the lower levels of cooperation required on the part of the child, relative to other dental treatments. It was therefore viewed as an appropriate option for children who are unable to cooperate with, or tolerate, other treatment approaches.

"Um, I think, um, where a child is not going to cope with either, um, the, um, placement of standard restorations or Hall crowns and the parent is very keen not to have teeth out, then I think that in particular is an area where we could, um, talk about that"

DP 4 (Dentist)

It was also suggested that SDF would not be limited to uncooperative children only but could also be used for adults with dental anxiety or special care patients.

"Yeah, adults with dental phobia, we also treat a lot of special care patients and I can see something like that would be very useful for them also"

DP 6 (Dentist)

A range of those interviewed agreed that SDF would be particularly beneficial where it might avoid or delay a child going under General Anaesthesia (GA) for dental treatment. Participants believed that parents would rather their child have black teeth regardless of whether this was posterior or anterior, if this would avoid a GA. A dental therapist who had experience of applying SDF on a three-year-old boy's anterior and posterior carious lesions commented:

"Uh, I didn't really need to convince her (the child's mother). She was happy to do it if it's a possibility of avoiding a general anaesthetic"

DP 5 (Dental therapist)

It was highlighted that the advantage is that SDF does not require any complex or advanced equipment. As a result, it could be particularly useful in deprived areas or countries with limited resources.

"I*t's of course entirely portable, it's very portable; it's very easy to use. Countries that perhaps have um, limited resources, limited funding, um, I'm sure it has a place there you know, it doesn't require suction and hand pieces and all the rest of it."*

DP 2 (Dentist)

It was also suggested that SDF would be particularly advantageous where a child has multiple carious lesions and treating all lesions requires several visits. It was suggested that applying SDF on all carious lesions as part of one appointment could be a time-saving and cost-effective way of managing such cases.

"you've often got the situation where a child has got lots of teeth that need treatment, um, so you could quite easily apply SDF on everything, even at one visit. And that would be a quick, cost-effective way of getting it done"

DP 1 (Dentist)

4.4.2.7 SDF compared to Hall Technique

The HT is becoming increasingly popular in children's dentistry and has been proven to be effective for managing carious lesions in primary teeth (Innes et al., 2017). There are similarities between SDF and the HT as both are considered to require less cooperation from children than traditional methods for managing dental caries that involve local anaesthesia injections and drilling. Also, some clinical situations sharing the same indications. This emerged strongly from the initial few interviews undertaken. As a result, the topic guide was adapted to specifically explore DPs perceptions of the advantages and disadvantages of SDF relative to those associated with the HT.

In terms of ease and comfort of application, interviewees considered SDF to be more comfortable for the child because SDF application is a simple process that does not require anything that the child would find uncomfortable, whereas the HT can be uncomfortable when seating the HT crowns.

“I mean certainly we do use the Hall crown a, a lot and you know, the Hall Technique and that’s, that’s very effective. But even then there are certain things you’ve got to do with it that maybe are slightly uncomfortable you know, putting the separators, actually seating the crowns, um, and they can be quite difficult, quite challenging if the crown, if it’s difficult to match the crown size to the tooth”

DP 8 (Dentist)

In terms of the extent of cooperation required by the child, DPs believed that the HT requires a higher level of cooperation, as fitting the HT crowns has more steps and it was considered to take longer and requite more cooperation that SDF application.

“Um, however, I guess the downside of the Hall crown is it does need a little bit more cooperation to do I think than SDF, um, because you need to seal it and remove cement and things like that”

DP 9 (Dentist)

“Silver diamine fluoride has the advantage that the main thing you need is for a child to sit still long enough while you paint something on their teeth”

DP 7 (Dentist)

It, however, was highlighted that a certain amount of cooperation was still essential for SDF application, in order to avoid inadvertently staining the skin.

“No, I think my only other concern is, um, one of the patient groups that you could use it with are the less cooperative children and my worry with SDF is if they do wriggle and you get it on the skin, it makes a mark. And, actually, therefore actually you need a level of cooperation so that, you know, you don’t get it on the skin. And that concerns me”

DP 4 (Dentist)

Another challenge with the HT relative to SDF, according to those interviewed, was the scenario where it is hard to fit the HT crown even though the clinical indication fits guidelines and the child shows a good level of cooperation. This can be due to either the tooth crown morphology or in cases of extensive carious lesions where marginal ridge breakdown has occurred and there is a lack of space between two adjacent teeth due to tooth movement. Participants suggested that SDF might be an alternative to HT in these cases.

"Um, we have some children where we have problems actually getting Hall crowns on, either the teeth are in a difficult shape for placing on the crowns or the caries and the way the caries has, er, caused teeth to close together means that it is difficult to get crowns on and it maybe that SDF gives us an alternative to just taking those teeth out or doing nothing"

DP 4 (Dentist)

Conversely, participants did suggest that when it comes to SDF, parents might be more sceptical about its effectiveness because the lesion is left open, and food might be retained in the area. The area also needs to be cleaned well during brushing, whereas if the HT was used, they may be more confident that because the lesion is covered it does not require the same level of follow-up care.

"The only thing about the Hall crown is at least the parent thinks it's covered so they don't have to pay so much attention to cleaning they would think in their head, you know, they think oh, it's covered up whereas they'd be more worried about, "Oh, you're just putting a paint on and darkening it, you haven't actually fixed the hole". So in their head they think why haven't you fixed the hole?"

DP 11 (Dentist)

4.4.3 Perceptions of parents'/children's treatment preferences

Two themes emerged under this theme. These are perceived concerns of regarding the treatment and perceived benefit of the treatment.

4.4.3.1 Perceived concerns regarding the treatment

A range of those interviewed believed that pain or discomfort during treatment was the primary concern for any parent in relation to their child's dental treatment. They advised that parents do not want their child to experience any pain during their dental treatment as they fear that such an unpleasant experience may create an anxious dental patient in the future:

"Um, yeah, so pain is one. If the patient needed … if the child needed to come in for work, one of the questions they always ask is, "Is there going to be a needle involved?" they're afraid that the kid will be afraid of dentistry from an early age, so anxiety, um, early on. Just knowing whether something is the right thing to do, if certain treatment is the right thing to do"

DP 10 (Vocational trainee)

A number of participants reported being concerned about the appearance of their child's teeth after treatment. However, it was suggested that parents would be willing to compromise on aesthetics depending on the individual situation:

"I think, for some parents, aesthetics are important, um, but not for all of them. Some can sort of see the balance that whatever works best for the situation"

DP 1 (Dentist)

It was suggested that prior to their child's dental treatment parents usually worry about whether their child would show a good level of cooperation, allowing the DP to proceed with the treatment:

"I think it concerns the parents about whether the child will cope with the treatments"

DP 4 (Dentist)

It was believed that parents generally prefer something convenient for both themselves and their children. Convenient to the parents was described as being non-time consuming and convenient to the child as being simple and easy to cope with.

"But I think parents also want something that's easy to do so the child doesn't get upset with treatment and, you know, is quite quick for them because they've obviously got to juggle lots of things, you know, like school and afterschool appointments and other children in the family. You know, as a parent myself of children, it's difficult juggling everything. So, they want something that's not time, you know, consuming."

DP 1 (Dentist)

4.4.3.2 Perceived benefits of the treatment

When DPs were asked what they believe parents see as the benefits of treating children's primary teeth, around half reported that having a healthy pain-free mouth and avoiding any complications in the future would be the main benefits for parents:

"The benefits to parents of having … obviously they probably see the benefits as stopping things before they get any worse, so if they've got active caries there,

they want it arrested before it becomes active pain or infection. Um, so I think that's the main benefit, sort of getting things under control and preventing any future disease"

DP 9 (Dentist)

A number of participants suggested that parents expect an additional outcome from their child's dental treatment, in addition to the general wellbeing of their child; an aesthetically restored tooth:

"Um, and then after that they would want to have the teeth restored so that the… again, sort of follows in the function, but then they would want to have teeth ideally restored so that they looked nice, um you know, so the, the aesthetic side of it came into it err, particularly on the front teeth"

DP 8 (Dentist)

However, some of those interviewed identified that there are still some parents who do not believe in the importance of treating children's primary teeth in the first place.

"Sadly, there are a lot of -- not a lot, but there are a group of parents out there that see no benefit in treating primary teeth at all, because they say, "Well, they're only going to fall out", so they don't see the point in treating"

DP 1 (Dentist)

It was suggested that this lack of awareness around the importance of treating primary dentition is not limited to parents alone, but that there are some DPs who are not fully convinced of the importance of treating primary dentition.

"and to be honest, I think, I think that feeling still exists with a lot of dentists as well, not just the parents you know, this idea it's a baby tooth, it'll fall out"

DP 2 (Dentist)

Participants presented diverse opinions around how parents may feel about the use of SDF. Some believed that parents would be reluctant to have SDF applied to their children's teeth due to the aesthetic outcome, while others suggested that parents may not mind the appearance of SDF treated carious lesions.

"The downside is it does look black so you will get some parents that'll say, "No, my kid's not having that done", I'm sure"

DP 1 (Dentist)

"*Speaking as a parent I think they would, they would go for that, I don't think they would mind so much"*

DP 3 (Dental nurse)

A range of participants suggested it was difficult to predict how parents would feel about SDF as not all parents necessarily share similar opinions.

"Uh, I think it would probably depend on the parent. You know, there's a lot of variability"

DP 12 (Dentist)

When considering some of the factors that may influence parents' decision-making about SDF treatment some suggested that fathers may be less concerned about the appearance of their child's teeth after treatment if the treatment was simple and pain-free, whereas mothers may be more concerned about the aesthetics of their child's teeth after treatment:

"I think generally if it was the mum coming in whether it was a boy or a girl that they're treating, they won't want them to have black teeth. Father would be more

chilled and the boy wouldn't care, he'd just be like, "Hah, I've got black teeth" but the girl would be more self-conscious generally. I don't know how much you remember growing up when you were small, I don't remember how I was when I was like four years old, five years old"

DP 10 (Vocational trainee)

It was also suggested that the age of the child at the time they were to have treatment may influence the decision-making process. Participants suggested that parents of younger children (age 6 or younger) would be less concerned about the discoloration, viewing younger children as less self-conscious as older children.

"I think they would be more acceptable with younger patients than older patients"

DP 7 (Dentist)

Participants also suggested that parents may take into consideration the position of the tooth. It was perceived that there would be less opposition to SDF if the teeth being treated were posterior.

"I think they would be, I think they would probably … probably be more accepting of SDF because it's easier to use. You know, if it's just back teeth"

DP 11 (Dentist)

It was also suggested that gender of the child could influence parents' decisions. However, regarding whether boys or girls might have different opinions, some of those interviewed suggested that girls are generally more self-conscious than boys, while others thought that the gender of the child would not influence the child's perceptions of SDF.

"You might imagine that a boy might not bother so much about the staining. Perhaps"

DP 6 (Dentist)

When considering how children may feel about their treatment options, DPs believed that children would generally prefer the least invasive treatment and, therefore, might choose SDF despite the discolouration.

"I think if you gave a child an option of having an injection and a filling or having something painted on, I think they would jump at having something painted on, definitely. You would have to explain to them carefully that it would be stained; some children would accept that, some wouldn't so you'd have to judge that carefully first"

DP 6 (Dentist)

This was caveated somewhat, by a belief that this may be more the case with younger children (age 6 or younger) as younger children may not be bothered by the staining, unless influenced by their parents expressing a different opinion.

"Yeah, younger kids wouldn't be as self-conscious. They haven't got the capacity to determine that, unless of course mummy says it's horrible-looking then they're probably not going to be very happy with it either"

DP 12 (Dentist)

"But I think as soon as children are getting towards the end of primary school into secondary school, I think, I think they might"

DP 2 (Dentist)

It was also suggested that older children may be more accepting of SDF for their posterior teeth, than for their anterior teeth and children who are more self-

conscious may also be affected by their social circumstances, taking into account factors such as the type of school they go to and the nature of peers they are surrounded by, before agreeing to receive SDF.

"Older than six or seven, I don't think they would want it on their front teeth. Back teeth, possibly, because it won't show. But front teeth, I don't think they'd want it"

DP 13 (Dentist)

"I think it, I think it depends on what environment they're in, so depending on what school they're at and the type of school that they're at, 'cause children can be cruel"

DP 3 (Dental nurse)

DPs interviewed believed that the black staining associated with SDF application would be the main barrier to its use from the parent/child perspective. There was an assumption that parents might not agree to use SDF for their children.

"The downside is it does look black so you will get some parents that'll say, "No, my kid's not having that done", I'm sure"

DP 1 (Dentist)

DPs suggested that due to the aesthetics, parents may fear that their children might be bullied at schools or nurseries having a detrimental effect on the child.

"Um, I think there are some children where, um, if their teeth go dark chocolate brown they might get picked on at nursery or at school and, um, that certainly -- I have met children where that has been an issue"

DP 4 (Dentist)

It was also suggested that parents may fear judgment from others, who may think that they are not looking after their child's teeth properly because of the black staining or SDF treated lesions.

"*So, they'll say, even though their child has got a mouth full of rotten teeth and we're trying to help them, "Oh, I don't want my child to have that. I'll look like I've not looked after them", that sort of thing"*

DP 1 (Dentist)

Since there is a chance of inadvertently staining the skin or the gingiva, it was reported that parents would probably be hesitant to agree to SDF treatment unless they trust the DP applying it.

"Um, and I think probably the biggest barrier that I'm gonna have with children is the idea that it will stain gingiva, or it will stain skin. So, I don't think a parent is going to be particularly open to using it if they don't trust the clinician who's doing it."

DP 7 (Dentist)

It was reported that DPs have encountered patients reluctant to receive any fluoride treatment. They believed that SDF would not be an option for these patients:

"There are some parents who believe fluoride is a poison and that is their belief and, um, despite the fact that you and I might think otherwise, if a parent holds these beliefs then, er, I do not think that we are -- we can point them in the direction of the research, er, literature on materials but we cannot force them to have something with which they, um, ethically disagree"

DP 4 (Dentist)

4.5 Discussion

This study was guided by the COREQ checklist. The researcher had undertaken training for conducting interviews and analysing qualitative data at the University of Oxford before starting the study. The researcher knew some of the DPs prior to the study, specifically those recruited through Dundee Dental School. However, no personal relationship between the researcher and the participants was established prior to the commencement of the study and therefore, there was minimal potential bias which could have influenced the interviews.

This qualitative investigation of DPs' knowledge, experience and acceptability of SDF revealed that DPs' knowledge and experience of SDF varied from being unaware of it prior to the interview, to having used it in practice. They believed the main advantages centred on its non-invasive nature and the low levels of child co-operation needed. The most common barrier reported was black staining of arrested lesions and DPs' concern about parent and child acceptance of this. It was agreed however, that parents and children may be more accepting of SDF and the staining associated with it, when applied on non-visible lesions or when used in place of more invasive treatments or GA.

The most common challenge reported was the provision of treatment for anxious and uncooperative children, which is understandable because managing children's behaviours in dental settings can be difficult (Sheller, 2004, Klingberg and Broberg, 2007). A SR suggested least one child out of ten had a level of dental fear and anxiety that hindered their ability to cooperate to receive dental treatments (Cianetti et al., 2017).

However, getting these uncooperative children to accept and sit through the appointments was also considered the most rewarding aspect. It was reported

that this can be achieved by communicating with the child and establishing a good relationship with them to eliminate any fears. Educating parents was identified as being extremely important. This is because, in children's early years, the family environment is where they spend most of their time and where most of their interactions and learning takes place. This is a critical environment for children to acquire knowledge, attitudes and habits related to oral health (Beljan et al., 2016).

Of those interviewed, all had some previous knowledge about SDF. Those working in a dental school setting or who had recently graduated were more aware of SDF use than those who had been practicing for longer. In terms of previous experience, only a few DPs had applied SDF before, and they were all employees at Dundee Dental Hospital and School. This may be because DPs working at educational institutions are more exposed to different and innovative treatment approaches.

The most frequently reported advantage of SDF was that its application requires a low level of child cooperation because it does not require administration of local anaesthetic. Therefore, it was thought that its use could help to acclimatise child patients to the dental environment, supporting them towards accepting more complex dental procedures in later visits. The simplicity of SDF application makes it possible to be applied as part of a child's first visit. This "familiarisation" visit could boost the child's confidence and result in a reduction in stress and an improvement in the patients' behaviour.

DPs thought that these advantages of SDF may reduce the likelihood of the child encountering any traumatic experience. This is particularly important because

past traumatic dental experiences, particularly in childhood have been linked strongly to the development of dental anxiety and dental phobia into adulthood (Hmud and Walsh, 2009). This, in turn, may affect their Oral Health-Related Quality of Life (OHRQoL) as it has been reported that children with dental fears have a higher risk of deterioration of their OHRQoL (Merdad and El-Housseiny, 2017).

The most commonly reported perceived disadvantage of SDF from DPs' perceptions was the permanent black staining of the arrested carious lesions caused by the formation of silver phosphate (Yee et al., 2009). Similarly, SDF can stain gingiva, oral mucosa and clinic surfaces (Horst et al., 2016). This means that DPs have to pay particular attention when applying it in situations where cooperation might be more limited. A few DPs reported that some patients reported experiencing a transient metallic taste if SDF gets in contact with their tongue. However, this side-effect resolves quickly and FV can be applied to the area of the tooth after SDF to prevent the unpleasant taste of SDF. This may also have the advantage of promoting further remineralisation.

DPs also reported some difficulties accessing approximal lesions and ensuring that SDF reached the entire lesion using a micro-brush. This can be overcome by using a smaller micro-brush or dental floss which makes applying SDF to the approximal lesions easier.

One other perceived disadvantage related to the commercial Riva Star, SDF product, is that it is available as a clear solution. This makes accidental spillages difficult to see until it is too late, and discolouration has occurred. Not all SDF

products have this issue, for example Advantage Arrest™ which has been marketed in the US is tinted blue, making it easier to spot any inadvertent spillage.

Adoption of new therapeutic approaches can be challenging. Several barriers to the uptake of innovative treatments have been identified, such as, lack of training, cost, lack of adequate evidence or consumer demand (Nelson et al., 2006, Pagoto et al., 2007). SDF is no exception; using SDF has not been taught nor introduced in most dental schools' curricula yet and, although it has been around for decades, has only recently become a popular topic in paediatric dentistry. Therefore, training events or workshops could be used to familiarise DPs with SDF, its uses and how to apply it, which may encourage its use in practice. To help with enhancing the uptake of SDF, it would be beneficial to raise awareness among DPs about the possibility of using, and when it is appropriate to use, an "off-license" product. According to the UK government website the prescriber can use off-label use of a product when they are satisfied that an alternative, licensed medicine would not meet the patient's needs and the use of an off-label product would serve the patient's needs better, based on the available evidence supporting its efficacy and safety (GOV.UK, 2014).

Fluoride varnish has been used in dental practice since the 1960s (Azarpazhooh and Main, 2008) and as a result, introducing a new fluoride agent may be a challenge. However, although the indications for SDF and FV overlap to some extent, they are some distinct differences in their indications too. Even though there is evidence around SDF's effectiveness for preventing carious lesions, it can also be used for arresting carious lesions in primary teeth. Moreover, it is recommended that FV to be applied after the application of SDF (Crystal et al.,

2017b). As a result, SDF and FV complement each other in a way, and SDF is not considered as a replacement for FV.

It should be noted that despite evidence of FV's effectiveness and published guidance for using it (Scottish Clinical Dental Effectiveness Programme, 2018), the majority of NHS Boards in Scotland have not met the UK Government's HEAT target for FV applications (NHS National Services Scotland Information Services Division, 2015). The reasons behind the low uptake remain unclear. Possible explanations are that some DPs are not convinced about the effectiveness of such preventive approaches, or some parents are reluctant to have fluoride therapy for their child.

Furthermore, it is not currently possible for DPs working in NHS practices in the UK to claim for the use of SDF as it currently does not appear in the SDR. This creates as additional barrier to its use.

DPs interviewed as part of this study reported that they believe the biggest barrier from parents'/children's point of view will be acceptance of the black staining associated with SDF application. This drawback is reported thoroughly in the literature and is speculated to be the one of the main barriers to the use of SDF in practice from parents' and children's perception (Gao et al., 2016b, Nelson et al., 2016, Duangthip et al., 2018a). The perceived reason behind this was that parents might fear that their child would be bullied at school or nursery.

DPs also believed that parents may hesitate about choosing SDF for their child because they fear they may be judged for their child's SDF-treated teeth appearance. It was suggested that parents may fear that people would think that they have been neglecting their child's oral health, even though in some cases

SDF can be the only option to avoid taking the child's teeth out. This suggests that there is a need to raise awareness about the fact that well looked after teeth does not always necessarily mean white teeth.

The potential inadvertent staining of gingiva and skin may also be a barrier for parents. However, good communication may go some way towards reassuring parents that the staining is harmless and will resolve spontaneously within two weeks with the normal exfoliation of the skin (Horst et al., 2016).

Some DPs reported encountered patients during their career who they refer to as "anti-fluoride". These people believe that fluoride is harmful despite the assurances of health organisations. There is a myth that water fluoridation causes a wide range of health problems, from bone cancer to dementia. Some even claim that community water fluoridation does not reduce tooth decay at all (Unde et al., 2018). It is likely that these people will be reluctant about receiving any fluoride treatment. However, raising awareness in a consistent manner by both the medical and dental societies on the significance of fluoride in promoting children's oral health, while addressing people's concerns might relief their fears (Ly et al., 2018).

In terms of what could facilitate using SDF in practice, with aesthetics being the most reported perceived barrier for its use, it is logical that overcoming or minimising the decolouration may be beneficial in facilitating the use SDF in the practice. Some studies have shown that potassium iodide (KI) can mitigate the discoloration caused by SDF (Nguyen et al., 2017). Riva star provide another set of capsules contain KI to be applied immediately after SDF. However, the

effectiveness of SDF+KI is still questionable compared to SDF alone (Zhao et al., 2017).

What could help to introduce SDF to parents according to the DPs interviewed as part of this study is having an SDF information sheet in the practice explaining the advantages, disadvantages, and expected outcome from such a treatment. This would allow a better understanding of the treatment, how it works and what other alternatives are available. It is thought that this would help the parents to judge whether the advantages overweigh the disadvantages in their individual situation and help them with the decision-making process.

National clinical guidelines are thought to be a main source for DPs in the UK to improve the quality of clinical decisions and assure them about the appropriateness of the treatments they provide (Bateman and Saha, 2007). Therefore, having a good quality evidence base around the effectiveness of SDF for managing carious lesions in primary teeth and introducing it into clinical guidelines may assure DPs about SDF's effectiveness and, therefore, encourage use. Having that in place might, in turn, support the introduction of SDF into the SDR allowing DPs to claim for applying SDF in NHS practices.

DPs believe that SDF would be particularly useful for pre-cooperative children i.e. very young children who cannot tolerate other treatments. This can be a transitional treatment while the child gets older and more cooperative or even a final treatment if the parents do not mind the discolouration. SDF's ease of use extends its uses to include uncooperative older children or even adults who cannot tolerate standard treatments for medical or psychological reasons i.e. frail elder or adults with physical disabilities or dental phobias. However, further

research to support the effectiveness of SDF in arresting carious lesions in permanent dentition is needed as most research on SDF conducted so far has focused on children. This unique indication of SDF could potentially help in reducing the referral of these patients to GA for dental treatments.

People in deprived areas who do not have access to dental care may also benefit from SDF because the procedure is portable and does not require any complex equipment for its application. It only requires an excavator to remove any gross debris from the lesions, cotton rolls, protective coating such as Vaseline, micro brush and SDF solution. Moreover, DPs believe that SDF could be beneficial for cases where a patient has several lesions that cannot be managed in one appointment and treating these lesions can take a considerable number of appointments over a long period of time, which might increase the risk of existing lesions to become symptomatic. Therefore, applying SDF on all lesions would arrest all lesions and control the disease while awaiting the completion of the treatment.

The similarities in clinical indications for both SDF treatments and HT raised a need to explore from the DPs perspective, the advantages and disadvantages of SDF treatments and the HT relative to one another. DPs believed that SDF treatments would be more convenient for the child than HT, as fitting the HT crown often requires placing elastic separators in the case of tight contact points with adjacent teeth and scheduling a second visit to fit the HT crown. Furthermore, seating the crown is not always a straightforward process. Moreover, the child might experience discomfort feeling after fitting the crown, however, this will resolve within 24 hours. Applying HT on a second primary molar adjacent to un-erupted first permanent molars, requires an extra attention from

the DP for the erupting first permanent molar not to become impacted under the crown margin.

In terms of the cooperation required for both approaches, since the application of SDF is easier and simpler than HT, it was perceived that lower levels of cooperation would be required when applying SDF and the child is only required to stay still for a few minutes to paint SDF on the carious lesion. However, any unexpected movement could result in a stain to the oral mucosa, skin or clinic surface therefore whilst lower levels of co-operation may be required than when fitting a HT crown there is still a degree of co-operation required. In addition, though SDF can be applied to several carious lesions even on two occluding teeth at the same appointment whereas HT cannot be fitted on two occluding teeth until occlusion is re-established with bilateral contacts. In term of the follow up for both treatment, all teeth treated with the HT or SDF should be followed up clinically and radiographically following the same protocols as conventional treatments, with SDF needs to be checked at 2-4 weeks after initial treatment to check the arrest of the lesions treated and be reapplied on biannual intervals to maintain the arrest of the lesions (Crystal et al., 2017b).

Interviewees had differing views around parents' attitudes toward using SDF for their child and it was identified that parents would not necessarily share the same opinions and they would probably take into consideration several factors before choosing SDF for their child. Age of the child was thought to influence the parents' choice with participants believing that parents of children aged six or younger may be more accepting of SDF for this age group rather than parents with older children. This was because they felt that younger children are not as self-

conscious as their older peers, and they probably would not mind the discolouration themselves either.

Position of the tooth that requires SDF application was also thought to influence the parents' choice. Participants suggested that parents may not mind the discolouration on their child's primary molars, but be more reluctant to using SDF on their child's front primary teeth. However, it is essential to explain to the parent the predicted time span of teeth that require the treatment and how primary incisors exfoliate earlier (around the age 6-8 years) than primary molars (around the age of 10-12 years) so that they take the predicted exfoliation into account as well, when choosing treatment options. This requires good communication in order for the DP to build trust, educate, and influence parents (Klein, 1993)

DPs had diverse opinions regarding whether the gender of the child would affect the parents' decision regarding the treatment chosen or not. Some believed that parents would be stricter when it comes to the appearance if the child was a girl and more flexible if the child was a boy. Others believed that gender may not influence a parents' decision. Similar differences in opinions where reported when DPs were asked whether a boy would have different perceptions of SDF treatment than a girl. There was a general feeling that there are no dramatic differences between the two genders. However, it was felt that there are boys who would be more accepting of the SDF treatment outcome than girls.

Those interviewed reported that pain is what concerns parents most when it comes their child's dental treatment, because experiencing any pain might create an anxious child (Hmud and Walsh, 2009). DPs believed that parents prefer a painless, convenient treatment for their child. Post treatment appearance was

thought to be important to some parents because dental appearance is part of body image and a child's satisfaction of their body image is essential for developing a self-confident individual (O'Dea, 2012).

Participants reported that some parents worry about whether their child will cooperate with the dentist enough to receive the required treatment. Some DPs also believed that some parents prefer the treatment to be convenient not only for the child but for themselves. Participants suggested that a simple treatment that can be conducted in a short appointment may be favourable to some busy parents that cannot free time for treatments that require a considerable number of visits.

Participants reported that they believe the main outcome parents wish from their child's dental treatments is a pain free, healthy mouth for their child. Having untreated carious teeth can result in serious complications, such as pain, oral infection, problems eating and sleeping and malnutrition, all of which would reflect on the general wellbeing of the child. However, DPs reported that that there are still some parents who are not fully aware of the importance of treating children's primary teeth.

However, there are a few caveats that should be kept in mind when interpreting the results of this study. Nine out of the 14 DPs who were interviewed had not had experience with SDF before and therefore, their views may change after applying it. In addition, because SDF was only introduced into the UK recently, DPs who had used it before, had limited experience and will not have had the opportunity to follow up patients over extended periods of time. Seeing patients over longer timeframes, allows clinicians to understand long-term outcomes

associated with treatment and gain deeper understanding of the impacts on the child and family. It could be the case that with greater experience and follow up with patients, the DPs' perceptions of the treatment may change. In addition, the interviews were conducted during the working day with busy healthcare professionals and it may be that they condensed their responses or were very focussed in their conversation due to time pressures. However, all participants completed the interview as planned and were asked if there was anything else they wished to add at the end of the interview. As a result, it is unlikely any important contributions were missed.

4.6 Conclusions

DPs were aware that SDF can arrest carious lesions but saw staining of the carious lesion as its major disadvantage and had preconceived beliefs that parents would find the appearance a barrier. They considered the application process to be simple, non-invasive and less challenging of child cooperation than other dental procedures, but that a minimum level of compliance would still be required. DPs believed that SDF is a valuable addition to their paediatric dentistry treatment procedures and were prepared to suggest actions that could be taken to reduce each of the barriers they noted.

The next chapter will explore parents'/children's perspectives, on treatment options for the management of dental carious lesions in children, with a focus on SDF.

4.7 Summary

Fifteen interviews with 14 DPs were conducted to explore their knowledge and experience of SDF, their beliefs about its use as well as their perceived barriers and enablers to using SDF in dental practice.

DPs' perceived advantages of SDF

- Lower level of compliance required of the child
- The potential for reduced referrals to Secondary Care
- Simple, easy and non-invasive approach
- Acclimatising children to the dental environment and help build a cooperative patient through their adult life

DPs' perceived disadvantages of SDF

- Black staining of arrested carious lesions
- Black staining of oral mucosa, skin, clothes, and clinics surfaces if contact is made
- Clear solution, which makes spotting accidental spillage difficult (some commercial products)
- Unpleasant or metallic taste
- Difficulties in accessing interdental posterior carious lesions

DPs' perceived barriers to using SDF

- Black staining of arrested carious lesions
- Staining the skin, the oral mucosa and the clinic surface if contact is made
- Getting DPs to use another fluoride agent other than FV
- The "off-label" use of SDF for arresting carious lesions
- Not listed in the SDR (for NHS practices only)
- People with strict beliefs about the safety of fluoride

DPs' perceived enablers to using SDF

- Information leaflets in practices to introduce SDF to parents/children
- Training and Continuing Professional Development events to educate DPs about SDF
- Listing SDF in the SDR (for NHS practices only)
- Improving the evidence base around SDF's use for arresting carious lesions
- Developing a way to minimise the staining effect of SDF

CHAPTER FIVE: PARENTS/CARERS' AND CHILDREN'S VIEWS OF SILVER DIAMINE FLUORIDE FOR THE MANAGEMENT OF CARIOUS LESIONS IN CHILDREN: A MULTI-METHODS STUDY

5.1 Introduction

Having investigated the evidence base around SDF and explored DPs' clinical experiences and preferences towards its use, this chapter will explore parents/carers' and children's preferences towards managing carious lesions in primary dentition with a focus on SDF.

Figure 5-1 Patients' values and preferences component of EBP

Hoffman and Glasziou (2016) suggest that "*Authentic evidence-based practice cannot occur if clinical decisions are made without consideration of the patient's preferences, values, and circumstances or if patients are not, at least, invited to participate in making decisions*". This can promote increased patient's knowledge and understanding of risks, improved clinician and patient communication and enhanced patient compliance.

The Journal of the American Medical Association (JAMA) user's guide to the medical literature defines patient preferences and values as: *"an overarching term that includes patients' perspectives, beliefs, expectations, and goals for health and life. We (JAMA) also use this phrase, more precisely, to mean the processes that individuals use in considering the potential benefits, harms, costs, and inconveniences of the management options in relation to one another"* (Montori et al., 2014).

Patients may have preferences and prioritised outcomes when it comes to choosing their preferred management option. However, access to individuals' preferences is not straightforward and they tend to form their preferences when they have to make a decision which is usually influenced by emotional and social factors (Epstein and Peters, 2009).

One side effect of SDF is that the carious lesion is stained black after application. However, it has been suggested that parents may view this discoloration as a positive indication that the treatment has been effective (Horst et al., 2016). In addition, a recent survey-based study in the US found that staining on posterior teeth was more acceptable than staining on anterior teeth and, although staining on anterior teeth was undesirable, most parents preferred this option to advanced behavioural techniques such as sedation or general anaesthesia (Crystal et al., 2017a).

It is not clear yet where the threshold for accepting this treatment and the undesirable effect of staining lies for parents/carers and whether they perceive any other barriers or enablers to using SDF. Furthermore, children's views of SDF have not yet been captured. This is despite the increasing emphasis on capturing the views of children within health services research to ensure that the treatments they are offered and their views on treatment outcomes are heard and, critically, are addressed (Marshman et al., 2015). This gap in evidence is needed to support decision making and treatment planning. It also presents an opportunity for an exploration of parents' and children's preferences toward using SDF to improve treatment decision making and contribute towards the implementation of this intervention into dental practice.

This chapter explores parents/carers' and children's opinions, views and acceptability of SDF as a treatment approach. To achieve this, qualitative interviews were deemed appropriate because they can provide a deeper understanding of a particular social phenomenon being investigated and are considered suitable where little is already known or understood about the topic under review or where comprehensive perceptions are needed from individual participants (Gill et al., 2008). Qualitative research with children has been considered a valid way to explore children's oral health related experiences and preferences (Marshman and Hall, 2008). To complement this qualitative aspect of the study, a questionnaire-based survey was undertaken in parallel to quantify participants' attitude toward SDF treatment and explore priorities parents place on the management options. This multi-methods approach can address research questions more comprehensively than by using either quantitative or qualitative methods alone and produce more thorough knowledge necessary to inform theory and practice (Tariq and Woodman, 2013).

For the purposes of presenting this work, the remainder of this thesis will refer simply to 'parents', as being anyone with the legal authority to consent to a child participating in this study.

5.2 Aim and objectives

The aim of this part of the thesis was to explore, with a focus on SDF, parents' and children's perspectives on treatment options to manage dental carious lesions in children.

The specific objectives were:

To explore with parents, for the carious primary dentition:

1. acceptability of SDF as a treatment approach (including barriers and enablers to use);
2. treatment preferences;
3. factors that influence their decision making around treatment options;
4. priorities they place on different management options.

To explore with children, for carious primary dentition, their:

1. views and acceptability of SDF as a treatment option;
2. previous dental experience.

5.3 Methodology

5.3.1 Study design

A multi-method study incorporating semi-structured face-to-face audio recorded interviews with parents and their children and a questionnaire-based survey was carried out (**Appendix *11***).

5.3.2 Ethical considerations

This study was approved by the Research and Development Management Department at NHS Tayside (IRAS ID: 254563, REC Ref: 19/ES/0042) (**Appendix *12***). Caldicott approval was obtained from NHS Tayside to allow access to personal data of potential participants for recruitment (Ref: IGTCAL6259).

5.3.3 Setting and participants

A range of parents and their children (aged four to 12 years-old, at the time of consent) attending the Child Dental Health Clinic at Dundee Dental Hospital and School were invited to participate. This part of the study took place between August 2019 and January 2020.

5.3.4 Sampling and recruitment

For the purpose of the recruitment this study was broken into two parts; study one: included the interview and the questionnaire and study two: included the questionnaire only for those were not interested in participating in the interview.

Potential participants were identified from the clinic list at the beginning of each day. During the child's appointment, the parent was approached by one of the DPs at the clinic, who explained the study briefly and introduced the researcher to the parents and their children.

The researcher described the two components of the study to the parents; study one (the interview and the questionnaire) and study 2 (the questionnaire alone). If they indicated an interest in a specific study, the researcher provided them with the relevant information pack. Parents interested in participating had the opportunity to call the research team if they had further queries, on the telephone number provided within the pack.

5.3.4.1 Study 1: Qualitative interviews and questionnaire-based survey

A purposive recruitment strategy sampling was used, based on eligibility criteria developed according to the research objectives and questions, to ensure that the sample was heterogeneous in terms of gender and age (Robinson, 2014).

Study 1's information pack included a PIS for parents that described the study in detail (**Appendix *13***), a PIS for children that was tailored to the child's age (preschool, P1-P3; and P4-P7) (**Appendix *14***), a reply slip to provide the

research team with their response, contact details and the best time to be contacted and a freepost envelope (**Appendix *15***).

Participants who took part in Study 1 returned the reply slip by putting it in a designated box at the reception in Child Dental Health Clinic at their next visit or by using the freepost envelope provided. The researcher contacted participants to arrange a convenient date, time and location for interview.

Prior to interview, the researcher discussed the study with participants, and they had the opportunity to ask questions. The written consent was read, explained and discussed with all participating parents to ensure they understood it before signing. The consent included critical and important actions that may be carried out during the interview (voice recording, details on interview nature, purpose of the interview, etc.) (**Appendix *16***).

The child assent process involved speaking to the child with the parent present. The assent process involved explaining to the child what would happen in the study, why it was being done and what the interview was about. It included answering any questions the child had about the study (**Appendix *17***). It is usually inappropriate to ask very young children (e.g. under 5's) to sign an assent form, however their wishes to take part or not were considered (Health Research Authority, 2013). The child's developmental stage was also considered. After the interview, each child received a £10 Love2Shop voucher as a token of thanks for participating. Parents were asked to complete the questionnaire after the interview but before leaving.

5.3.4.2 Study 2: Questionnaire-based survey

The questionnaire part of the study's information pack included a PIS for the parents that described the study in detail (**Appendix *13***), the questionnaire (**Appendix 18**) and a freepost envelope.

Participants who took part in the study 2 returned the completed questionnaire using the freepost envelope provided or by putting it into a designated box at the reception in Child Dental Health Clinic at their next visit. Participants' consent was implied by their completion and return of the questionnaire. The participant information sheet highlighted that participation was voluntary and that they should not feel pressurised to participate. They were also informed that they were free to withdraw from the study at any time and that their responses would only be used for this piece of research.

5.3.5 Withdrawal procedure

Participants had the right to withdraw from the study at any stage without providing a reason. No one withdrew from the study.

5.3.6 Data Collection

5.3.6.1 Qualitative interviews

Semi-structured face-to-face interviews conducted by the researcher in a suitable venue within Dundee Dental Hospital and School. Open-ended questions and probing were used. The parent was interviewed first, then the child, with both being together in the room for both interviews.

An interview topic guide (**Appendix *19***) was informed by the literature and was developed to explore from the parent and child perspective, using age-appropriate language. Prior to the interview, participants were given the opportunity to ask any questions and if they were happy to take part, a written informed consent was obtained before the start of the interview.

Questions explored, the acceptability of SDF; perceived barriers and enablers to its use; factors that influence decision-making regarding the treatment options and the influence of previous dental experience. Children's interviews explored views about SDF treatment and their previous experiences of visiting the dentist.

Interview schedules were piloted with two parent-child dyads prior to starting the study to ensure they were clear to the target populations. Small revisions around the use of language used were made to the schedules following this process. Data from the pilot interviews was not included in the analysis. Data collection was carried out until saturation was reached i.e. when no new themes, categories or explanations were emerging from the data.'

5.3.6.2 Questionnaire-based survey

The questionnaire explored the priority placed on the management of dental caries when considering all of the different treatment options. It looked at what parents thought about their child's previous dental appointments. The questionnaire also aimed to assess the level of importance parents placed on having their child's carious primary teeth treated and their acceptance of SDF treatments. To explore the influence of aesthetics and parents' acceptance of the black staining associated with SDF treatment, clinical photographs of front and

back teeth before and after SDF treatment were presented. Parents' views of the aesthetics of SDF treated teeth were explored by asking them to agree or disagree with a number of statements. Parents were also asked to prioritise a number of factors that influence their decision making around how their children's teeth are treated. At the end of the questionnaire, there was a question posed to the child about how they feel when they are visiting the dentist. The parent could complete this question with the child, or the child, if old enough, could circle the answer by themselves.

This questionnaire was adapted from ones developed for a similar study conducted in the US, but adapted to be relevant to the UK population, in terms of the language used and to the context of the study aims (Crystal et al., 2017a). The questionnaire was initially piloted to test content validity with a small group sample similar to the target sample, i.e., parents in the waiting area at the Child Dental Health Clinic (n=5). A brief discussion was conducted with the parents upon completing the questionnaire to gather feedback. The majority of the feedback was positive, however some repetition in questions was highlighted. In order to address some words were capitalised and highlighted in red to ensure clarity.

It was estimated that a sample of 110 participants could be recruited based on the allocated timeframe for this part of the study and the average number of children visiting the Child Dental Health Clinic daily. However, it was acknowledged that this would be dependent on patient attendance, willingness to participate and response rates.

5.3.7 Data Handling and Analysis

5.3.7.1 Qualitative interviews

Thematic analysis was undertaken using the framework approach as a broad guide to organise and classify data according to key issues, concepts and emerging themes (Ritchie and Spencer, 2002). Similarly, to data analysis in the previous chapter, all interviews were recorded and transcribed in verbatim. All identifiable data were anonymised before they were transferred to the transcription service. Audio recordings and transcripts were uploaded into NVivo to facilitate data management. All real names were pseudonymised in the transcripts during the analysis.

The Consolidated Criteria for Reporting Qualitative Research (COREQ) was followed to guide analysis and reporting of the data (Tong et al., 2007). The five stages of data analysis using the framework approach were then conducted; Familiarisation, identifying a thematic framework, indexing, charting and mapping and interpretation (Ritchie and Spencer, 2002). (Details of each stage can be found in the previous chapter, (page 102).

A coding framework was developed following the initial review of three transcripts. This was then assessed by one of the PhD supervisors who was not involved in conducting the interviews. Development of the codebook was an iterative process with adaptations made through discussion as appropriate.

5.3.7.2 Questionnaire-based survey

Analysis was conducted using Statistical Package for the Social Sciences (SPSS) software (IBM Corp, 2017), a comprehensive system for analysing

quantitative data. Descriptive statistics and analyses of frequencies were used to describe the basic features of the data and provide simple summaries about the sample and check the distribution, central tendency and dispersion.

Data assembling

All data was managed in accordance with the Data Protection Act in 2018. Hence, the confidentiality of data and anonymity of the participants were ensured throughout the process. Data assembly means gathering together all the checked, edited and coded questionnaires, and entering the values for each variable for each case into data analysis software. This is usually achieved in a framework of rows and columns for storing the data called a data matrix. Data was first inputted into an Excel spreadsheet before being exported to SPSS.

Double entry of 10% of all data was conducted by two individuals in order to check the accuracy of the data entry i.e. ensure that there were no discrepancies between the hard copies and the electronic dataset. The error rate was 0.75% which is an acceptable error rate and there was no need for a second round of data checking (Atkinson, 2012).

The completed questionnaires were locked in lock protected cabinet. All online information records were held in a password protected network with a back-up held in a secure office.

Missing data

If a question was unanswered, the researcher, when entering data into the Excel sheet, entered ‘Not applicable’ for the missing value. The amount and distribution of missing data were analysed for each question and each were treated similarly.

Any completed questionnaire with ≥ 5% missing responses was omitted from analysis. If there were ≥ 2% but less than 5% of items missing from individual participants' responses, then they were treated as though the data was missing at random (Schafer and Graham, 2002). The method imputation using the mean recommended by Huisman was used to replace data judged to be missing at random (Huisman, 2000). Therefore, any missing data was replaced using the mean of the non-missing values of the same question.

5.4 Results

5.4.1 Qualitative interviews

Eleven group interviews with 11 parent/child dyads were conducted. The 11 parent participants comprised three fathers, seven mothers and one grandmother. All children were regular attenders and of the 11 children, 55% were boys. The age of child participants varied from six years-old or younger (n=4), 7-9 years-old (n=3) and over nine years-old (n=4). Interviews ranged in length from 15 to 25 minutes (total interviews time 229 minutes). Table 5-1 summarises the characteristics of participants.

Table 5-1 Characteristics of parent and child participants

Parent's gender		Child's gender		Child's age	
Female	8	Female	5	Six years-old or younger	4
Male	3	Male	6	7-9 years-old	3
				Over nine years-old	4

Previous dental experience varied across all of the child participants, but all children interviewed had previously had regular check-ups. Two children had not experienced any intervention other than fissure sealants. Five children had undergone GA for multiple primary teeth extractions, and one had previously required a local anaesthetic for teeth extractions. Three children had received fillings, one of which had required a root canal treatment for a permanent tooth. Three had received the HT and two children had previously received SDF treatment at Dundee Dental Hospital.

Parents of children who had multiple teeth extracted under GA described the experience as traumatic for both themselves and their child. In addition, they suggested that they felt that an excessive number of teeth had been extracted during the procedure.

"I was angry, I was angry, I was angry, 'cause he, he was sitting there crying for mum and dad and we were there and there's nothing I could've done er, he didn't want put to sleep. The, the nurses, give the nurses their due, they tried everything, give him a gas until he fell asleep. It's when he woke up was when the pain kicked in, and to see a child going through a lot of pain after this being done, getting them all taken out"

(Parent 9, father to a 10 years-old boy)

"it was, "Well, if we're going to take the problem tooth out, then we may as well take the one that looks even worse," although that one had never given her any pain or, um, problems. And then it had spread to – oh, there was, er, spotting or shadows on other teeth and they thought they're going under, so all of them go! So she had five teeth out"

(Parent 4, mother to a 6 years-old girl)

Children who could recall their GA experience, reported it as being unpleasant:

“Do you know what I didn’t really like? When they went into the thing when I got put to sleep, I don’t like that”

(Boy 8, aged 7 years old)

How the child coped and adapted post-treatment was also raised by these participants who spoke about having to adapt to eating with multiple teeth missing, often resulting in a specific soft diet and missing school lunches.

“I think it was just quite traumatic with the extent at which it had to be done, you know, eating afterwards, she’s used to eating with molars, to have no back teeth was interesting”

(Parent 4, mother to a 6 years-old girl)

“while my teeth were getting better, I did go to school but I had lunch at home”

(Girl 4, aged 6 years old)

Parents of children who had received the HT reported being satisfied with the HT application, despite it being slightly uncomfortable for the child. They reported however not considering the HT to be a straightforward process due to the complexities of choosing the right size and the time taken to carry out the procedure.

“I think when they were putting the crown on there was a lot of, “Is it the right size? Is it not the right size?” and trying to get the right size to fit over the top. And then they had to squish it and, you know, it was a bit of a… it took quite a while, you know? If I remember rightly it was a little bit uncomfortable when they were pushing it on, trying to fit it”

(Parent 8, mother to a 7 years-old boy)

Children who had received the HT suggested that having the crown fitted was not difficult, even though that there was some minimal pain.

"…so I went and got the crown. It didn't really hurt, it only hurt, like, a tiny bit because he really hard pushed on my tooth to stick it on, but it never really hurt"

(Girl 5, aged 9 years old)

Parents of the children who had previously received SDF treatment reported the application process was simple, quick and easy for the child. The treated lesions turned black, but the discolouration did not concern these parents given that the SDF treated teeth were posteriors.

"Er, I thought it was great. Er, the fact that the teeth turned black did not bother us in the slightest because we knew that it was doing him good, and it was the best thing to put on ….. maybe because they were at the back, they're not very visible so you wouldn't see it unless you were actually in his mouth, looking to see it. Er, but for what it done, it was great. It took away his discomfort and his pain, it was fantastic"

(Parent 7, father to a 10 years-old boy)

Older child participants also reported SDF treatment to be easy and did not appear concerned about the discolouration. When asked about the black staining on their teeth one participant commented:

"I don't care. I don't care"

(Boy 7, aged 10 years old)

5.4.1.1 Parents' views of SDF

Two overarching themes emerged from interviews about SDF with parents: perceptions of SDF and decision making with several subthemes under each theme.

5.4.1.1.1 Perceptions of SDF

The parents who were interviewed expressed varying views about SDF treatment. Although many acknowledged the advantages, they also identified disadvantages that would create barriers to its use in children. Two subthemes emerged under this theme. These were perceived advantages of SDF and aesthetics.

Perceived advantages of SDF

A range of parents believed that SDF treatment could be particularly useful for both anxious and uncooperative children whose lack of cooperation may limit the possibility of receiving some interventions.

"I think it's a great treatment for kids, especially young kids that are apprehensive about coming to the dentist or the dentist sort of, er, looking in their mouth and things like that"

(Parent 11, father to a 5 years-old boy)

Parents perceived SDF to be a non-invasive treatment that does not include any procedural parts that the child would find stressful, such as local anaesthetic or use of the air rotor instruments. It could therefore be a useful entry point to the dental environment for children.

“It’s less invasive, he doesn’t have to have any needles or anything like that”

(Parent 11, father to a 5 years-old boy

“Um, I just think it’s less… for Jack, he was, when he first started coming here, a little bit apprehensive about going to the dentist and getting new treatments, and I think it would be more, kind of, scarring for him to start getting these major treatments happening at such a young age, compared to getting that painted on”

(Parent 7, father to a 10 years-old boy

Parent interviewees also suggested that an added advantage of SDF was the possibility of delaying or avoiding a GA where the child would lose several teeth and then need to cope with a situation which may affect speech, diet or the quality of oral health.

“then she would keep her, um, chewing would maintain normally, you know, she wouldn’t be learning how to eat without teeth, to re-learn how to eat with teeth. It’s also good to keep, um, a muscle memory on how to brush your teeth when they’re there, because if they’ve all gone, then obviously that changes. Yeah”

(Parent 4, mother to a 6 years-old girl

It was also suggested that SDF treatment was advantageous in promoting good oral health with the child being encouraged to look after their teeth after having the treatment in order to minimise the pain.

“it made a massive difference to Jack when he got that put on. He was kind of scared to brush his teeth because he was in that much pain, and then after that product was put on, he could brush his teeth. It helped him help his other teeth that were going to be staying”

(Parent 7, father to a 10 years-old boy)

Aesthetic

A range of parents were concerned about the permanent black staining of the arrested carious lesion, especially if the treated tooth was anterior. It was even suggested that an SDF treated tooth would look worse than the original untreated carious lesion. Parents thought that the advantages of SDF could outweigh the disadvantages, namely, the discolouration in some specific situations.

"I guess it looks worse to me, it doesn't look like there's been a problem solved but obviously there is"

(Parent 2, mother to a 5 years-old boy)

"Because it looks like decay itself"

*(***Parent 6, mother to a 10 years-old boy)**

"the only downside to it is it doesn't look very nice with it turning black, um, but I suppose, um, it's a small price to pay to save the tooth rather than, um, having to have it taken out or even a filling or crown put on it"

(Parent 11, father to a 5 years-old boy)

Parents suggested that developing a way to mask or minimise the black staining would be useful in improving SDF acceptability. They believed that SDF would undoubtedly be one of the most appreciated treatments in paediatric dentistry should there be a way to overcome the discolouration.

"I mean, the only thing with the SDF treatment is the look of it, and if they were able to apply that treatment, um, to front teeth without it going black, um, then it would be an amazing treatment for, er, for kids to get done"

(Parent 11, father to a 5 years-old boy)

5.4.1.1.2 Decision making

Another overarching theme was “decision-making”. Parents did not seem to have a clear opinion about choosing SDF for their child or not. There were many considerations that could impact upon their decision-making in relation to their child’s dental treatment. In addition, parent participants suggested measures that could be used to encourage the uptake of SDF and ways to sway both parents and children to view it as an acceptable treatment approach.

Perception of others, visibility, self-conciseness, duration, alternative approaches, communication, financial considerations and child tolerance

Perceptions of others

A range of parents believed that the discolouration, especially if visible on anterior teeth could result in the child feeling uncomfortable or anxious when they speak or smile and hence may be more susceptible to school bullying.

“I think it’s more when it’s at the front um, front teeth and they’re smiling and it’s very obvious that it’s… they’re black um, I think I would be more nervous. Um, I think because I think children um, other children can be unkind and I think it can cause children to feel uncomfortable or nervous about their smile um, if they were very obviously looking like this at the front”

(Parent 10, mother to a 9 years-old girl)

“then the next thing, a kid’s at school with black teeth… I think I’m all about the anti-bullying, and this to me would lead to bullying”

(Parent 5, grandmother to a 9 years-old girl)

However, the prevalence of bullying at their child's school seemed to influence parents' decision making around the use of SDF for their child. If the school had frequently reported bullying problems, parents seemed less keen on SDF.

"He's quite lucky in that the school he goes to, there's very, very little bullying or anything like that happens, they're really good at controlling these kind of things, um, so it probably wouldn't be a barrier for us, personally. I think for some people, it probably would be"

(Parent 7, father to a 10 years-old boy)

It was also suggested that people usually associate black-stained teeth in adults with drug abuse and that this may be reflected towards children too. This fear of what 'others would think' may introduce an additional consideration for parents when deciding whether or not to support the application of SDF on their children's teeth.

"Yeah. I mean, black teeth nowadays is associated with drug abuse in adults, you see adults with black teeth, nine times out of ten, they're addicted to some kind of drugs. So this is obviously… this is a hard one. Nowadays, when you think about the drug abuse and the kids that are actually involved as well in drug abuse today, know what it is, know exactly what this is, black teeth in adults. The kids do know that, unfortunately. It's not a nice thing"

(Parent 5, grandmother to a 9 years-old girl)

In a similar vein, it was believed that parents may be judged by others if their child has black-stained teeth. They feared being thought of as neglecting their child's health, because a blackened tooth may appear similar to an untreated carious lesion and people may not be able to differentiate. In those scenarios the parents

believed that they would rather have the teeth extracted. According to them, this would mean they would be less likely to be judged by others, as people would assume that the teeth have exfoliated earlier than normal.

"But yeah, I'd be more worried about other people's… what they think, which is bad, you know? I suppose it's a risk having anaesthetic and getting your teeth out, but I would rather that than people judging me"

(Parent 8, mother to a 7 years-old boy)

It was believed that SDF could be more acceptable approach if people had greater knowledge and awareness about it as a treatment option. With greater awareness there may be less chance of being judged by others and therefore, parents would be less apprehensive about choosing SDF for their child.

"I think, I mean, maybe more to the future when there's more people know about it, you know? I mean, at the minute, I wouldn't know anything about it. As I say, if you see teeth like that, you would just think, "Oh, they're bad! They're bad teeth and they've not been to the dentist." But maybe more to the future, once it's been around a while, people know more about it, they'd maybe understand what it was and they maybe wouldn't judge so much, you know?"

(Parent 8, mother to a 7 years-old boy)

Visibility

The visibility of the SDF-treated carious lesion in the mouth seemed to be the most influential factor when it comes to whether a parent would choose SDF treatment for the child. A range parents considered SDF to be an acceptable management option, if it were to be applied on their child's back primary teeth since it would not be visible when the child speaks or smiles. Some parents

commented that the arrested carious lesions do not look worse than amalgam fillings:

“if it is in a back tooth, a back molar, then it’s the equivalent of one of the old iron or dark fillings”

Parent 4, mother to a 6 years-old girl

However, there was far more opposition to SDF if it were to be applied on front teeth. Few parents said that they would not mind their child getting SDF on their front teeth if it would stop the progression of the carious lesion and avoid any further intervention. It was thought that the aesthetic outcome of SDF treatment on the front teeth was unacceptable and parents would not opt for SDF for their child’s front teeth since other people can spot the discolouration easily:

“Hmm, it looks awful! It looks awful. …. certainly on a front tooth, I wouldn’t want that on my child”

Parent 6, mother to a 10 years-old boy

Size of the carious lesions especially in the case of anterior teeth, was of importance to some parents because bigger lesions would stand out more. They considered that SDF is a possible option for an anterior carious lesion, if the lesion was relatively small and not terribly noticeable.

“But like, if it was just a small pit like that and knowing that he’s not gonna have it long because his new teeth are coming in, I would probably say, “Yeah, fair enough,” you know?”

Parent 8, mother to a 7 years-old boy

Self-consciousness

Parents believed that the age of the child may be an important factor in deciding whether to choose SDF treatment. They deemed that younger children would not be as self-conscious as older ones and would not mind the black staining, and therefore, discolouration may be less of a barrier. Whereas for older children, parents reported having to think carefully before choosing SDF, due to the potential for bullying from their peers.

"It wouldn't have bothered me before, now that he is at school, it would worry me that other children might pick up on that and that might be an issue, only because of children's behaviour. Yeah"

(Parent 2, mother to a 5 years-old boy)

"She is nine, and I think that at that age you become a little bit more um, insecure and you're, you're more aware of what people um, think um, and kids also at that age can be unkind, and, so I think that if, if it was gonna cause children to be teased more that would be something that I would want considered"

(Parent 10, mother to a 9 years-old girl)

Gender of the child did not appear to influence parents' decision-making regarding the use of SDF on their child, and parents did not suggest that self-consciousness would differ from boys to girls.

"I think it would be the same for both, to be honest. Yeah. I mean, again, probably, if this was the only option to stop the decay and, you know, like, she couldn't cope with any sort of treatment, then it's… yeah"

(Parent 3, mother to a 10 years-old girl)

Duration

Another factor that seemed to affect parents' decision making was how long the child would keep the SDF-treated tooth for after treatment. Parents had conflicting opinions about how that might affect their decision. Some thought that if the teeth were to be lost within a short period of time i.e. less than six months, they would consider SDF treatment otherwise, they would consider alternative approaches.

"I would probably say, "Yes, put that on it," because I know they're not gonna be there long, they're going to fall out, they're close to getting new teeth. But if it had been, like, maybe a year or two years ago and it's a long time 'til he gets his second teeth, you know, and he was gonna have this for a long time, I would probably think, "Hmm, maybe not." You know?"

Parent 8, mother to a 7 years-old boy

Conversely, some believed that if the tooth to receive the SDF treatment would fall out in few months, they would rather just take the tooth out and if the tooth was likely to last longer they would opt for SDF.

"If she was on the crust of her new teeth coming through and it would only be, like, two or three months, I would say, "Och, yeah, take them out then." What's the problem? Young kids at that age do lose their teeth anyway. But if it was going to be a longer period of time, six months plus without teeth, I would say, "Nah, get this treatment done"

Parent 5, grandmother to a 9 years-old girl

Alternative approaches

Parents tended to take the other options available for managing the carious lesion alongside SDF into consideration when choosing the treatment. Some parents who were less accepting of SDF showed more flexibility if SDF was the last resort that could save the front teeth from extraction. Those parents believed that having a black-stained tooth was better than not having tooth at all.

"Um, I would still be, um, kind of… I would lean towards doing it rather than losing the teeth"

Parent 4, mother to a 6 years-old girl

Most parents reported that they would choose SDF, albeit hesitantly, if it avoided the child undergoing GA for extractions or other treatments, because they did not want to put their child through the risk of a GA.

"Mhm. I wouldn't want her put to sleep for her teeth to be filled or treated. I'd rather that she had that, the SDF because there's such a risk with general anaesthetic. Well, not a massive risk but there's still a risk with GAs isn't there"

Parent 1, mother to a 5 years-old girl

Even if the other option was conducting the treatment under laughing gas which is less invasive than GA, parents tended to choose SDF.

"Just don't want any drugs or chemicals put in her that I don't have to… you know, like the laughing gas, it's still… I know it's not a bad thing or anything like that, but no, I think I would just rather that these were coated on her baby teeth and we're gone for six months!"

Parent 3, mother to a 10 years-old girl

A range of parents insisted that they would never choose SDF for their child's front teeth and considered the outcome unacceptable. According to these participants, extracting the teeth would be a more acceptable management approach than applying SDF and having a visible, black-stained tooth.

"Yeah, that's awful. I would rather he got put to sleep and them taken out, yeah. I would rather not have them"

Parent 8, mother to a 7 years-old boy

When parents were asked if they had to choose between HT or SDF for their child, since both techniques overlap in some clinical situations, a range of parents preferred their child to have SDF. The rationale for this was that from the aesthetic perspective, the crowns are silver, cover the whole tooth and not very aesthetic either where as SDF only covers the carious part of the tooth. Furthermore, applying SDF would be simpler and more convenient for the child.

"I think when they were putting the crown on there was a lot of, "Is it the right size? Is it not the right size?" and trying to get the right size to fit over the top. And then they had to squish it and, you know, it was a bit of a… it took quite a while, you know? If I remember rightly it was a little bit uncomfortable when they were pushing it on, trying to fit it, so I mean, this would be a lot simpler. You know, the back teeth, getting that stuff on, it would probably be a better option"

Parent 8, mother to a 7 years-old boy

Communication

It was reported that parent would prefer to take their child's preferences into account when choosing the treatment. They did not want to force the child to receive any treatment they are not keen to get, if it was possible.

“I think as a, as a parent yeah, I mean it would obviously depend on… because it’s work to be done to the child, so I would want to have their opinion on it, and I would never force something. Um, if there was, if there was two options and a child felt more comfortable with one option then I would, I would obey that”

Parent 10, mother to a 9 years-old girl

It was suggested that the dentist was the expert and reported having full trust in them. They were happy to choose whatever treatment the dentist believed to be the best option for the child.

“I suppose I very much always go by what the dentist would recommend”

Parent 6, mother to a 10 years-old boy

Financial considerations

It was suggested that the cost of the treatment to the NHS would be something parents would consider before choosing the treatment. If there were two management options with similar success rates, they would prefer the more cost-effective treatment approach.

“Um, and also I am interested in what it costs um, the NHS and, and things like that because that’s something I think that we do need to be responsible citizens and if there are treatment options that are going to be more cost effective for the NHS then I do think um, that it’s, that it’s our duty to consider those”

Parent 10, mother to a 9 years-old girl

Child tolerance

It was reported that some children have sensitivity issues towards strange smells or tastes and would not be able to tolerate a treatment which included either. Parents suggested that this would add an additional barrier to the use of SDF.

"The only thing he has a problem with, he's got, like, sensory things, you don't like tastes and smells and things. So, if it's certain varnishes and the coatings and things that they're using, if they taste funny or smell funny, he's like, "No!" He's more frightened of that than anything else"

(Parent 8, mother to a 7 years-old boy)

5.4.1.2 Children's views of SDF

Younger children interviewed were shy and generally less talkative than the older children, especially at the beginning of the interview. These younger children tended to be more responsive to yes and no questions than questions probing for more exploratory responses. Children were shown pictures of SDF treated teeth as part of the interview and they described them as "rotten", "weird", "silly", "ugly" or "disgusting". One overarching theme, "child's acceptability of SDF" emerged from the interviews with children and encompassed three sub-themes: visibility, peers' perception and previous experience.

5.4.1.2.1 Child's acceptability of SDF

Visibility

When asked how they felt about having similar treatments on their teeth, a range of children seemed unfazed about the black staining if it was to be on their back teeth, believing that others would not see or notice the black staining.

"Um, on the back, that's okay, kind of. I don't mind to have [it] because people wouldn't really, like, see it when, like, um, like, when I'm like, talking or anything, because it's in my, like, one of my back teeth, so they wouldn't really see it"

(Girl 5, aged 9 years old)

“If I had to have this on my back teeth, I would be okay like that”

(Boy 8, aged 7 years old)

“I, I wouldn’t mind it as much being in the back teeth”

(Girl 10, aged 9 years old)

Despite the relative positivity about the application of SDF on posterior teeth, most children interviewed for this study were not keen on having SDF on their anterior teeth. This was due to its visibility and they did not want to have what looked like a rotten tooth. If the lesion was fairly small however, there was less opposition.

“Um, if they were at the front, I wouldn’t really like it. If it was just a little at the front, then that would be okay, like that one”

(Boy 6, aged 10 years old)

“No, I wouldn’t have it. But if it’s small, I would have it…But if it was a big bit like that, no way”

(Boy 8, aged 7 years old)

“Er, if it was a little hole, I wouldn’t mind if it was gonna stop a hole”

(Girl 10, aged 9 years old)

A range of children reported that they would be unwilling to accept SDF treatment for their teeth at all, regardless of whether it was to be applied on a posterior or an anterior tooth. They reported they would prefer to have the teeth extracted.

“Probably just get them taken out”

(Girl 3, aged 10 years old)

"Will you be okay with this one? Because obviously we can't see it, only the dentist would see this"

(The researcher)

"No"

(Boy 2, aged 5 years old)

Boys and girls did not appear to exert different attitudes about having their teeth treated with SDF. Both genders reported similar perceptions of the treatment.

A range of children interviewed were not accepting of having SDF applied to their anterior teeth due to its visibility. Their reasoning behind this was a fear that others would comment on their appearance and they may be picked upon by their peers. One child who had previously suffered from bullying at school commented:

"Oh, the front teeth, no, no ….. Absolutely not because they look not that nice. I wouldn't like that because it will look silly, because I think I'll get bullied. And then people will just go, like, "Amy, what are your teeth like? They look ugly." I think they'll say that"

(Girl 5, aged 9 years old)

Another child added that a friend of theirs at school had a black discolouration on their teeth, and they believed they were picked on at school because of it. However, it was not possible to confirm whether that was a result of SDF treatment or not.

"Uh, yeah, I think so, because people might, um, think that something's, like, black on their tooth and they don't know what it is and they'll… like, 'cause one of my friends had it and people sort of made fun of them. So they had, like, some black stuff on their teeth and, um, my friends made fun of them"

(Boy 6, aged 10 years old)

Based on child responses, there was a general feeling that older children were more aware of the discolouration and how that could lead to being picked on than younger children. It was suggested that younger children may be less self-conscious or worried about the implication or reaction from others of having black staining on their teeth.

""If they see them and they think it's rotten then I think they'd possibly laugh if they're in like the older classes, but otherwise if it was friends they would try and support them"

(Girl10, aged 9 years old)

"And how about younger children like five-year-old children"

(Researcher)

"Um, I don't say… I wouldn't say as much as them. I… if they didn't know what it was, so they wouldn't laugh I don't think as much""

(Girl10, aged 9 years old)

"they might but I wouldn't 'cause I would just be like, "Oh, oh my god," and it's like, you know what I mean? Like, I'm shocked because it looks so bad"

(Boy 8, aged 7 years old)

Previous experience

Previous dental experience appeared to influence children's opinions in relation to dental treatment. The majority of children who had experienced multiple teeth extractions under GA, had found their experience to be painful. They reflected that they would choose SDF if it meant they could avoid a further GA.

"Yes, I would prefer that one. Yeah, 'cause getting all those teeth pulled out I couldn't go through all that pain again, oh, that was so sore"

(Boy 9, aged 10 years old)

On the other hand, one child seemed less bothered about undergoing a GA and reported that they would rather have GA again than have SDF treatment. This child participant had also previously had Hall Crowns applied and said they would prefer to have further Hall Crowns than SDF. The rationale behind this appeared to be based on knowledge of what to expect and a fear of the unknown with SDF.

"Plus, I've experienced it before, I know what it already feels like. And I know it sounds weird, but I kind of liked it anyway"

(Boy 8, aged 7 years old)

This qualitative aspect of the study with 11 parent/child dyad explored parents' acceptability of SDF; including perceived barriers and enablers to its use in addition to factors that influence decision-making regarding the treatment options. Children's interviews explored views about SDF treatment and their previous experiences of visiting the dentist.

The next part of the study; the quantitative aspect explored the priority placed on the management of dental caries when considering all treatment options and assessed the level of importance parents placed on getting their child's carious primary teeth treated and their acceptance of SDF treatments.

5.4.2 Questionnaire based survey

5.4.2.1 Demographics

One hundred and twenty-seven questionnaires were distributed to parents who visited the Child Oral Health Clinic at Dundee Dental hospital during the period August 2019 to January 2020. Sixty-three questionnaires were returned completed providing an overall response rate of 50%. However, two

questionnaires were omitted from the analysis because over 5% from the responses were missing in each questionnaire. This resulted in 61 questionnaires included in the analysis.

Sixty-four percent of those who responded were females. In relation to the children that respondents were answering the questionnaire about, 58% were boys. The mean age was 7.9 years and children were distributed across school years as follows: Preschool 14.8% (n=9); P1-3 29.5% (n=18) and P4-7 55.7% (n=34).

5.4.2.2 Oral health behaviours

When asked about their children's oral health behaviours, 1.5% of parents reported that their child brushed their teeth or had their teeth brushed for them three times a day, 79% reported this happened twice a day, 18% reported once a day and 1.5% said that their child never brushes their teeth.

All 61 parent responders said that their child had visited a dentist before the visit where they were handed the questionnaire. Of the 61 children that these parents were reporting on, 38 had previously had carious lesions, 33 of which had been managed by using crowns or fillings.

5.4.2.3 Assessment of the child's previous dental experience

As part of the questionnaire, parents were asked to rate their child's overall experience at the dentist on a scale of 0 (Not good) to 10 (Good). The last question within the questionnaire asked parents to ask their child to select the face that best represented how they feel when they go to the dentist to have their teeth checked.

Parents assessments of their child overall dental experience echoed to some extent what children themselves reported feeling about their visits to the dentist. The majority of parents and children rated the child's dental experience positive, although more children thought that their experience was neutral compared to parents. Figure 5-2 demonstrates how parents perceived their child's overall dental experience, while Figure 5-3 shows how children themselves felt about their visits to the dentists.

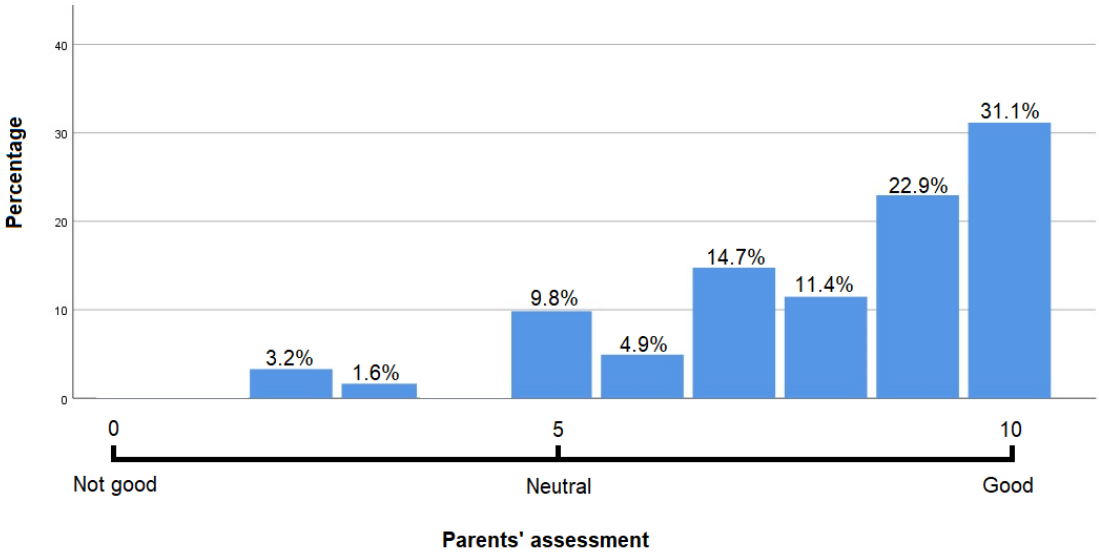

Figure 5-2 Parents assessment of their child overall dental experience (n=61)

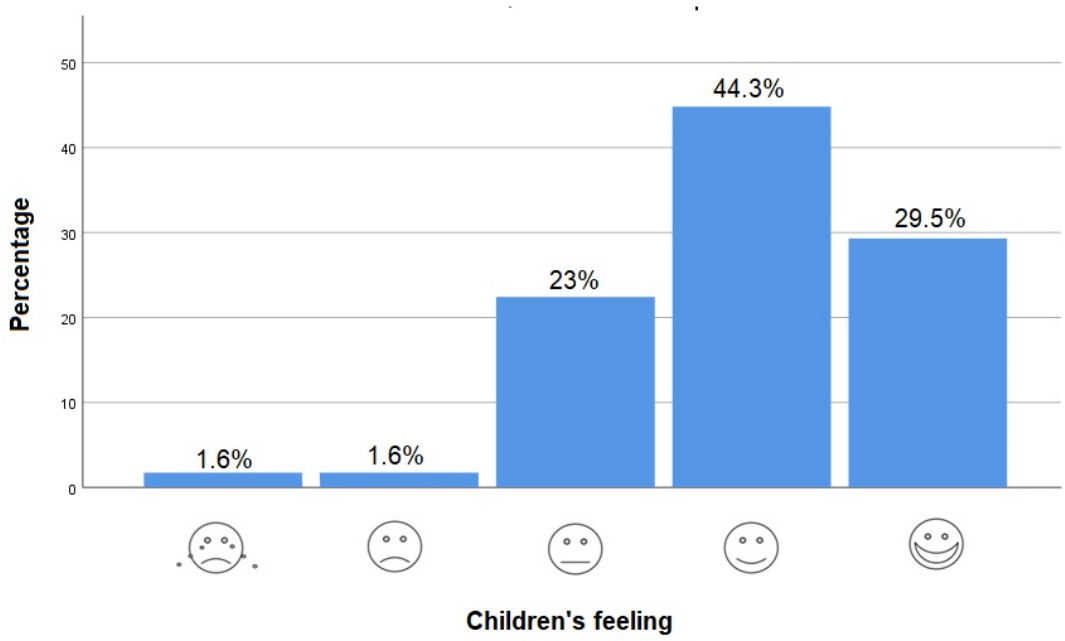

Figure 5-3 How children feel when they go to the dentist to have their teeth checked (n=61)

5.4.2.4 Parents' attitude toward treating primary teeth

The vast majority of parents (around 95%) strongly agreed or agreed that it was important to treat carious primary teeth. When specifically asked about this importance in relation to front and back primary teeth, almost 94% of parents strongly agreed or agreed that the appearance of children's front primary teeth after dental treatment was important, whereas 65% of parents strongly agreed or agreed that it was important that their child's back primary teeth looked good after treatment Table 5-2.

Table 5-2 The Importance of treating and aesthetically restoring baby teeth according to parents

		Percentage distribution of responses			
		Strongly agree (1)	Agree (2)	Disagree (3)	Strongly disagree (4)
I think it is important to fix baby teeth		34.4%	60.7%	4.9%	0%
I think it is important that my child's baby teeth look good after dental treatment	Front teeth	19.7%	73.8%	4.9%	1.6%
	Back teeth	9.8%	54.1%	29.5%	6.6%

5.4.2.5 Parents' attitude toward SDF

The questionnaire contained clinical photographs of carious lesions before and after they were arrested with SDF, with brief description of the SDF treatment procedure. Parents were asked how they would feel about the discolouration caused by SDF treatment if it appeared on the front and back primary teeth.

Around 20% of parents “strongly agreed” that the discolouration was acceptable on their child’s primary back teeth and this percentage tripled for people who “agreed” to the same statement. Over 40% “disagreed” and around 35% “strongly disagreed” that discolouration would be acceptable on the primary front teeth Table 5-3.

Table 5-3 Parents’ attitudes toward the discolouration resulted from SDF treatment

		Percentage distribution of responses			
		Strongly agree (1)	Agree (2)	Disagree (3)	Strongly disagree (4)
I would find the discolouration from SDF to be acceptable if my child had cavities on their	Back teeth	19.7%	60.7%	18%	1.6%
	Front teeth	3.3%	21.3%	41%	34.4%

Parents were also provided with ten scenarios based on their child’s behaviour and cooperation when attending the dentist, and asked to either strongly agree, agree, disagree or strongly disagree with the statements.

Just over 40% of parents “strongly agreed” or “agreed” that they would choose SDF for their child’s back teeth, even if their child were cooperative and did not show any behavioural barriers to receive a traditional treatment, compared to around 15% in the scenario when it was their child’s front teeth. However, this acceptance increased to almost 60% and 20% for posterior and anterior teeth,

respectively, if the child was upset, but cooperative enough to get a traditional treatment done.

If the child was cooperative but crying, over 65%, and 30% of parents, respectively, “strongly agreed” or “agreed” that would choose SDF for their child’s back and front teeth.

The reported acceptance of SDF increased to almost 85% and over 55% for their child’s back and front teeth, respectively if the child kicked or screamed and could not cooperate enough to receive a traditional treatment.

The last scenario hypothesised that conventional treatment was not an option due to lack of child’s cooperation and extraction of the child’s teeth under GA was the only other solution. In this situation, over 90% and 70% of parents “strongly agreed” or “agreed” that they would choose SDF application for their child’s back and front teeth, respectively, if this could avoid the child undergoing a GA (Table 5-4).

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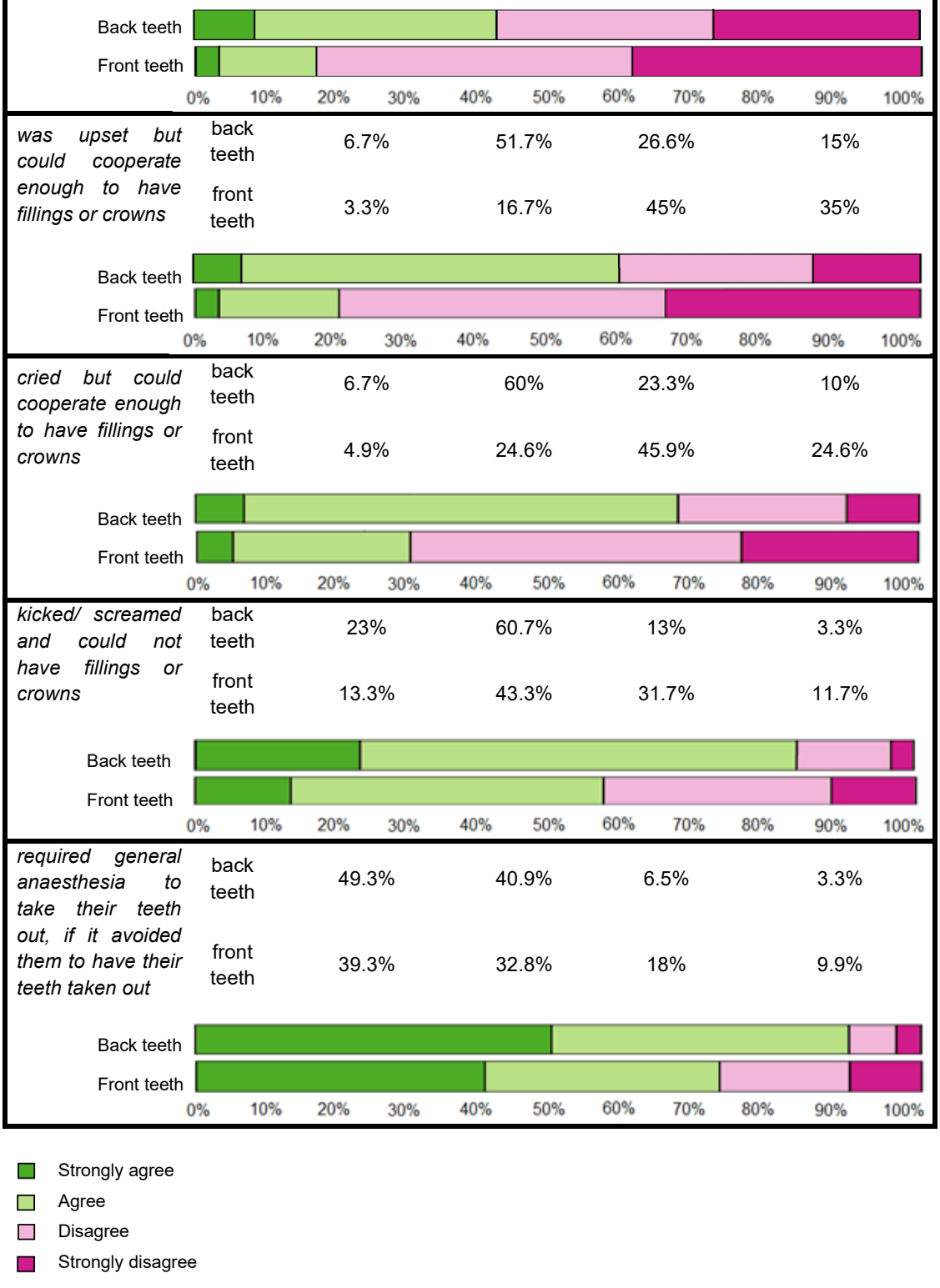
Table 5-4 Distribution of parents' responses to questions investigating SDF acceptability in different scenarios

I would choose SDF if my child		Strongly Agree	Agree	Disagree	Strongly disagree
was fine to have fillings or crowns	back teeth	8.3%	33.3%	30%	28.4%
	front teeth	3.3%	13.3%	43.4%	40%
was upset but could cooperate enough to have fillings or crowns	back teeth	6.7%	51.7%	26.6%	15%
	front teeth	3.3%	16.7%	45%	35%
cried but could cooperate enough to have fillings or crowns	back teeth	6.7%	60%	23.3%	10%
	front teeth	4.9%	24.6%	45.9%	24.6%
kicked/ screamed and could not have fillings or crowns	back teeth	23%	60.7%	13%	3.3%
	front teeth	13.3%	43.3%	31.7%	11.7%
required general anaesthesia to take their teeth out, if it avoided them to have their teeth taken out	back teeth	49.3%	40.9%	6.5%	3.3%
	front teeth	39.3%	32.8%	18%	9.9%



5.4.2.6 Factors influencing parents' decision-making

Parents were also asked to consider and prioritise factors that are important to them when deciding how their children's primary teeth are treated. They were provided with a list of eight factors and asked to number these from the most important (1) to the least important factor (8). They were also able to add other factors they believed to be important when it comes to choosing a dental treatment for their child. No respondents added additional factors to those included within the list.

The mean for each of the eight factors was calculated in order to prioritise based on the perspectives of the participating parents. The full ranking is provided in (Figure 5-4). Parents included in this survey, identified the success rate of the dental treatment to be the most important factor when considering their child's dental treatment, this was followed by the appearance of the child's tooth after dental treatment and then the avoidance of a drilling procedure. The least important factor as rated by these respondents was the ability to limit the treatment to a single appointment, followed by the length of the appointment.

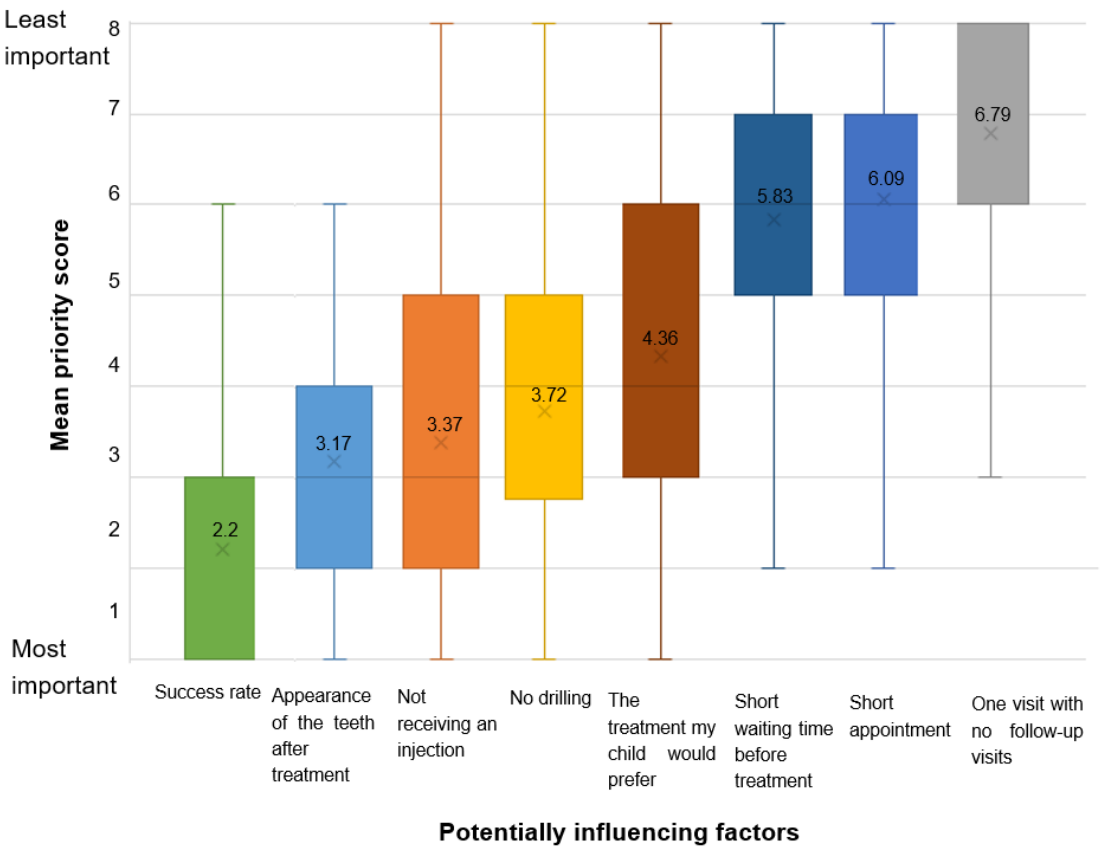


Figure 5-4 Mean level of priority placed on individual factors that might influence parental decision about their child's dental treatment (n=61).
The ends of whiskers present minimum and maximum values.

5.5 Discussion

The qualitative component of the study was guided by the COREQ checklist. The researcher had undertaken training for conducting interviews and analysing qualitative data and had experience in qualitative research having undertaken the previous study with DPs. The researcher did not know the participants before the study and no personal relationship between the researcher and the participants was established prior to the commencement of the study. In addition, the researcher was not a clinician at the Child Oral Health Clinic where the participants were recruited from and therefore, child participants would not have viewed the researcher as their dentist which may have influenced their answers during the interview.

This study investigated parents' and children's acceptability of SDF in addition to their preferences around treatment options and found that parents believed that SDF would be valuable for uncooperative children. However, they and their children were concerned that the SDF-induced black staining on front teeth could instigate bullying at schools and, therefore, were more accepting of SDF treatment on less visible back teeth. Parents reported increasing acceptance of SDF as child cooperation deteriorated. Older children seemed more concerned about the discolouration.

Parents assessment of their child's previous dental experience aligned with children's views, with the majority reporting their experiences to be positive. In addition, the vast majority of parents (95%) acknowledged the importance of treating carious primary lesions, perhaps reflecting an awareness of the value of the primary dentition. Although not specifically explored, one potential explanation for those who thought it was not important to treat primary teeth may be that parents believe that these teeth will exfoliate and be replaced with permanent teeth eventually. This finding is at odds with some of the previous work in this area, (Nagaveni et al., 2011, Setty and Srinivasan, 2011, Chhabra and Chhabra, 2012, Setty and Srinivasan, 2016) which revealed a lack of knowledge and awareness of importance of the primary teeth among parents. It should be noted however that these studies were conducted 5-10 years ago in different populations and cultures.

The appearance of their child's teeth after treatment was of importance to the majority of parents. This is in line with the previous studies explored parents' perception of the of the importance of the aesthetic aspect of the primary. dentition. Parents were critical of their child's teeth appearance (Shulman et al.,

2004) or unaccepting of discoloured front primary incisors (Woo et al., 2005) or concerned with the appearance of primary teeth with fluorosis (Clark et al., 1993). However greater importance was placed on the front teeth than on the back. The perceived implications of having un-aesthetic front teeth were explored in the qualitative part of the study and parents expressed concerns about how that may instigate bullying or that they may be judged as parents for neglecting their child's oral health.

Parents' views and acceptability of SDF were explored in both the interviews and questionnaires. Interviewee findings identified the most commonly reported advantage of SDF treatment was the benefits associated with treating uncooperative children. It was agreed that this non-invasive treatment should limit distress to the child and, therefore, could be useful to help acclimatise children to the dental environment and get them to accept more complex procedures in the future.

Parents also pointed out that SDF would be beneficial in avoiding or delaying the use of GA. Parents whose children had required GA in the past stressed this point and suggested that if SDF had been an option for them previously they would have chosen SDF, despite the discolouration. This was because the GA experience had been traumatic for both the children and the parents. This parental attitude toward GA is supported in the literature (Podesta and Watt, 1996, Atan et al., 2004). A qualitative study conducted in 2006, exploring parents' experience of their child's dental GA reported that parents were troubled that their child needed a GA. It went on to say that while some parents struggled to accept the use of GA, others believed it was actually superior to conventional treatment. Nonetheless, all parents reported some levels of anxiety, fear or worry associated

with their child undergoing dental treatment under GA (Amin et al., 2006). These concerns associated the GA probably justify the high acceptance rate of SDF reported in the questionnaire if SDF could avoid the child to go under GA for teeth extractions.

Children who had undergone dental treatment under GA also reported finding the experience unpleasant. They were troubled by being put to sleep and the pain experienced after the procedure. This feeling among children who had received dental treatment under GA was supported by Rodd *et al* (2014) who conducted a qualitative study with children to explore their views of having teeth out under GA. They revealed that children felt scared and worried before their admission, mainly coming from not having an idea about what was going to happen to them in addition to feeling discomfort from the intravenous cannula. Using a different methodology, Baghdadi *et al* (2020) utilised children's drawing as a projective measure to understand their experiences of dental treatment under GA. The main concern reported for children during the pre-operative period was that they were forced to prepare for an unknown experience, which provoked stress. The paper also reported that extraction of multiple teeth and the inconvenience of the anaesthetic gas mask were troubling for the child.

Parents expressed concerns about the aesthetic outcome of the treatment especially if this was visible. The rationale for this was that the appearance of SDF-treated teeth could increase the chances of the child being bullied at school or nursery. The prevalence of bullying at their child's school could, therefore, have an impact on the parents' decision. Children themselves were also concerned about the discolouration claiming that they would be picked on if they had black stained teeth. Older children i.e. seven years or older seemed more concerned

and aware that having black teeth could instigate bullying at school. This is plausible given that physical appearance is the most frequently cited reason for bullying. Globally, 15.3% of students who have been bullied, reported being made fun of, because of how their face or body looks (Unesco, 2018).

In a similar vein, it was commented on the association of black teeth with drug abuse. It is unarguable that substance misuse could have a deteriorative impact on oral health, and can be represented in rampant caries and severe periodontitis (Yazdanian et al., 2020). Discoloured SDF treated teeth may resemble the typical oral appearance of drug misusers, and people may not differentiate between the two. This may influence parents, especially in areas with a higher prevalence of drug misuse.

Related to this, parents also reported a fear of being judged by others if their child had black teeth even if it was not a carious lesions but an SDF-treated tooth because, again, people may not differentiate between the discolouration and a rotten tooth. Therefore, parents may fear that others may think that they have been neglecting their child's oral health, even though in some cases SDF could be the only option to avoid taking the child's teeth out. These parental fears did not seem to be specifically attributed to SDF treatment only, Maguire *et al* (2020) reported that parents had raised similar concerns about the crowns in their child's mouth being a visible sign of failure in their parental responsibilities. This barrier was considered one which could be overcome through an increased awareness of SDF treatment and its staining effect. In these instances, people would be more aware and accepting of the idea that a well looked after tooth does not necessarily mean white tooth. It may also be worth introducing this concept to children in order to mitigate against bullying.

This may be one reason why there is higher parental acceptance of SDF for back teeth than for front teeth, as identified from the survey data. Around 20% “strongly agreed” and 60% “agreed” that the discolouration was acceptable on back teeth, whereas over 40% “disagreed” and around 35% “strongly disagreed” that discolouration would be acceptable on the primary front teeth, perhaps because parents probably understood that the staining would be much less visible in back segments. This echoes the findings of previous studies exploring parents’ perceptions of SDF (Crystal et al., 2017a, Kyoon-Achan et al., 2020) and was supported by the interview findings with children as part of this study which identified that regardless of gender or age less opposition was shown for SDF on back teeth compared with front teeth.

Parents’ acceptance of SDF was influenced by the child’s cooperation with the dentist i.e. Parents acceptance of SDF increased when the child was getting more apprehensive to receive a conventional treatment. This finding was similar to this of which our questionnaire was adapted from (Crystal et al., 2017a). They reported that parents’ acceptance level of SDF increased as the child required more advanced methods of behaviour management.

Parents also reported that the age of the child was something they would take into consideration as older children may be more self-conscious and less likely to accept the treatment. It was suggested that younger children may not be as self-conscious as their older peers and may not mind the discolouration as much. In contrast to this, a study exploring perceptions around dental aesthetics in paediatric dentistry found that younger children (aged 2-7 years-old) have the perception that beautiful teeth are shaped and white, while ugly teeth are shapeless and have cavities in them (Vale et al., 2009). Furthermore, children at

age six years-old were capable of appreciating the aesthetics of the restorations for their anterior teeth (Pani et al., 2016).

The gender of the child did not seem to be a factor that influenced parents' decision making regarding SDF treatment. It was suggested that this may have affected parents' views before, but currently there is a feeling that boys and girls are considered similarly. Interview data suggested no real difference between genders' perceptions, with boys and girls sharing similar beliefs about SDF treatment. This finding is supported by a study which explored body image perception. In this study the results suggested that boys' and girls' body image perceptions show similar trajectories (Heron et al., 2013).

The parents had diverse opinions about the influence of the exfoliation of the SDF-treated tooth on their decision making. Some believed they would consider SDF if the teeth were going to fall out within few months, while others believed that they would consider SDF if the tooth was going to stay in the mouth for longer. Therefore, it is essential to explain to the parent the predicted time span of the teeth that require SDF treatment and how primary incisors exfoliate earlier (around the age 6-8 years) than primary molars (around the age of 10-12 years) for example. This would allow parents and children to take this into consideration when choosing treatment options.

The survey data identified that parents perceived the success rate of any dental treatment to be the most influential factor for them when choosing dental treatment for their child. Therefore, it is crucial that parents are informed about the success rates of the possible treatment approaches. Using SDF for arresting carious lesions shows an arrest rate of (65-91%) (Seifo et al., 2019). This makes

the success rate of SDF similar to other approaches', such as HT (over 93%) (Innes et al., 2017) or ART (over 65%) (de Amorim et al., 2018).

The appearance of the teeth after dental treatment was the second priority. This is particularly important when considering SDF due to the unfavourable aesthetic outcome. Parents also prioritised the avoidance of use of the air rotor (drilling) or injections relatively highly. SDF, in addition to HT and ART are minimally invasive treatment options and therefore preferable to more conventional treatments, in that respect.

Parents reported taking their child's preferences into consideration if possible. This was also supported by interview data which suggested parents were not keen to force a treatment on their child unless it was the only available option. The length of waiting time was less of a priority to parents. However, SDF could be taken into consideration in the scenario where there is a long wait for the preferred treatment option, and therefore, SDF could be a useful option in preventing asymptomatic lesions from becoming symptomatic.

Parents were least concerned about dental treatment that required several appointments. This may be because all children, regardless should attend the dentist every six months for a check-up. This is particularly essential for children who receive SDF which needs to be applied every 6 months to maintain carious lesions arrest (Seifo et al., 2020).

It should be noted that some of the themes to emerge from the interview data perceptions of others, visibility and self-consciousness are very much interlinked, and focus on the overarching theme of the aesthetic outcome of SDF treatment. Whereas other themes, such as communication, financial consideration and

child's tolerance were standalone and probably applicable to other dental treatment not only SDF (Table 5-5).

Themes	Sub themes	Topics within the theme
Perceptions of SDF	Perceived advantages of SDF	Minimal child's cooperation required Non-invasive stress-free treatment The possibility of saving the tooth from extraction Promoting good oral health
	Aesthetics	The black staining of arrested lesions Minimising the staining to improve acceptability
Decision making	Perceptions of others	Bullying at schools or nurseries Other people's judgment
	Visibility	The position of the tooth effect on parents' decision
	Self-consciousness	Child's age/gender's impact on parent's decision
	Duration	The time for the tooth's exfoliation
	Alternative approaches	Saving the tooth from extraction Avoiding GA Choosing between SDF and HT
	Communication	Child's preferences Dentist's recommendations
	Financial considerations	The cost on the NHS
	Child tolerance	Child's sensitivity to strange smells or tastes

Table 5-5 Themes emerged from the interviews with parents

To the researcher's knowledge, this is the first study to use multi-methods to explore parents' and children's acceptance of SDF. Previous studies have explored the acceptability of parents alone. This study also investigated how that acceptance level varies according to the child's behaviour when receiving treatment. The acceptance of SDF staining was greater for back teeth than for front teeth. Acceptance level increased as the child showed behavioural barriers to receive conventional treatments.

A purposive sampling framework was used for the qualitative component to ensure that the sample was heterogeneous in terms of children's gender and age. Socioeconomic level, educational level and residence location (urban, suburban, or rural) were not investigated in this study. Therefore, it was not possible to assess whether these variables could have an impact on the level of parental acceptance of SDF.

Participants were recruited through Dundee Dental Hospital only. However, patients' values and expectations are unlikely to vary considerably across the whole population. It should be noted however, that the primary aim of qualitative research is to gain a greater understanding of opinions and trends and not necessarily identify issues that are generalisable. The analysis of the results of the qualitative component relies solely on the researcher. However, to minimise the bias a number of interview transcripts were double coded independently by the researcher and one of their supervisors.

5.6 Conclusions

Parents believed that SDF would be particularly useful for anxious and uncooperative children and the simplicity of the application procedure could make SDF an entry point to more complex procedures. However, they were concerned that the SDF-induced black staining on front teeth could instigate bullying at schools or nurseries and it was suggested that this could subject parents to judgments and accusations of child neglect. Children also expressed concerns about being picked on by their peers, if they had front discoloured teeth. Therefore, parents and children were more accepting of SDF treatment on less visible back teeth. Parents reported increasing acceptance of SDF as child cooperation deteriorated and SDF was most acceptable if it could avoid the need for taking the child's teeth out under GA. Younger children seemed less concerned about the discolouration. Gender of the child did not seem to influence parents' decision nor the child's preferences regarding the use of SDF.

Although parents highlighted some disadvantages and barriers associated with SDF application, they appreciated the potentials of SDF treatment especially for uncooperative children.

5.7 Summary

The study aimed to explore parents' and children's views and acceptability of SDF. Eleven parent/child dyads participated in the qualitative aspect of the study and 61 completed and returned the questionnaire.

Parents' views did not differ from those of Dental Professionals. Parent participants believed that SDF would be particularly useful for anxious or uncooperative children and the simplicity of the application procedure could make SDF an entry point to more complex procedures.

Parents however expressed similar concerns to those of Dental Professionals that SDF-induced black staining could trigger bullying at schools or nurseries, if applied on front teeth, and suggested that this could subject them to judgment by others and accusations of neglecting their child's oral health. The children who were interviewed also expressed concerns about being picked on by their peers if they had discoloured front teeth.

Parents and children were more accepting of the SDF on non-visible back teeth. Parents' acceptance of SDF also increased if their child was less cooperative with the dentist or if SDF treatment avoided extractions under a general anaesthetic. In agreement with Dental Professionals' preconceived ideas, younger children appeared less concerned about the discolouration and the gender of the child did not seem to influence parents' decision-making nor the child's preferences regarding using SDF.

CHAPTER SIX FINAL DISCUSSION, CONCLUSIONS AND RECOMMENDATIONS FOR FUTURE RESEARCH

6.1 Discussion

The overarching aim of this thesis was to explore the use of SDF for managing carious lesions in children within the framework of the three components of EBP; Best Research Evidence, Clinical Expertise and Patients' Values and Preferences. To achieve this, the project was divided into three research objectives which map directly to these three components of EBP (Figure 6-1).

These three research objectives were:

1. To conduct a comprehensive review of the evidence for SDF for managing carious lesions.
2. To explore DPs' views and acceptability of SDF.
3. To explore parents' and children's views and acceptability of SDF.

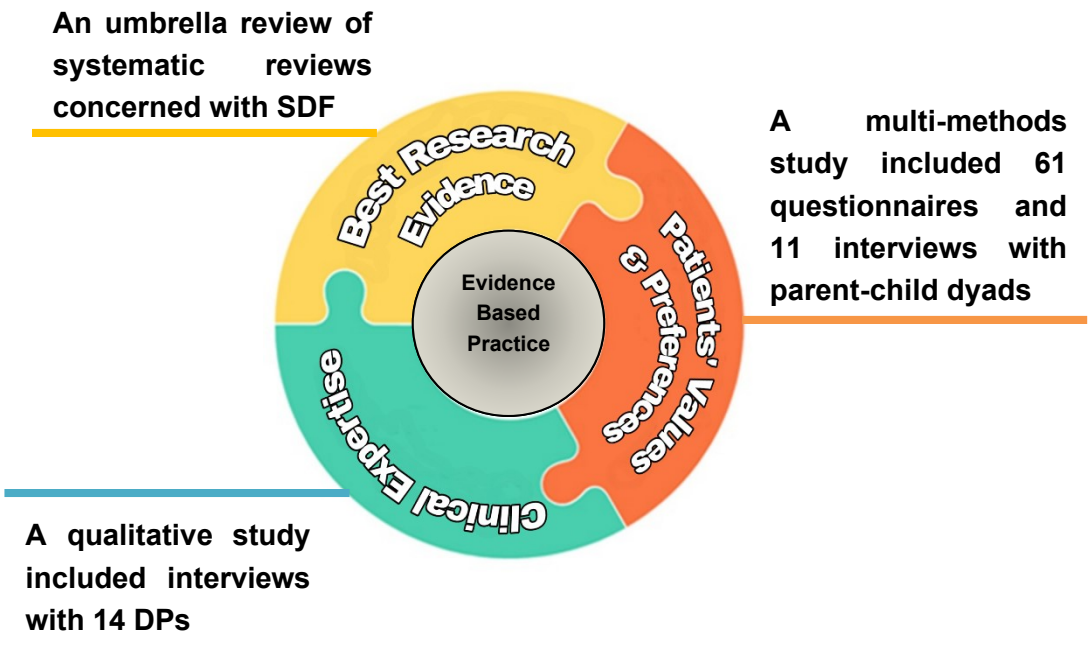


Figure 6-1 The study methodology covered the components of EBP

Research objective 1

In order to meet the project's first objective, to conduct a comprehensive review of the evidence around SDF, an umbrella review of SDF for managing carious lesions was carried out. This umbrella review assessed SRs of SDF for: The breadth of evidence assessed in the SRs; The risk of bias of the SRs; The effectiveness of SDF for managing carious lesions in children and adults, and adverse events associated with SDF application.

The umbrella review identified that the evidence for using SDF for managing carious lesions in children was well established. Eleven SRs were included within the umbrella review. Overall, all SRs reported that SDF was effective in managing carious lesions. However, earlier ones tended to overstate conclusions around SDF's effectiveness given the limited number of trials they were based on, and the SRs' high risk of bias.

For root carious lesion prevention and arrest, the SRs were based on only four clinical trials. However, all trials were assessed as high quality in the SRs.

For coronal carious lesion prevention, it is noteworthy that the number and quality of studies included in the SRs was low, identifying a gap in the evidence base around SDF for coronal carious lesions prevention. For coronal carious lesion arrest, an increased number of SRs have reported stronger evidence to support SDF use in the primary dentition.

Research objective 2

In order to address the project's second objective, to explore DPs' views and acceptability of SDF, semi-structured interviews with 14 DPs from NHS Tayside and NHS Grampian were undertaken. The interviews investigated DPs' existing

knowledge and experience of SDF and their perceived advantages, disadvantages, barriers and enablers to the use of SDF for the management of carious lesions in children.

Interviews revealed that DPs' knowledge and experience of SDF varied significantly, from being unaware of it prior to the interview, to having used it in practice. They saw the main advantages centring on its non-invasive nature and the low level of patient co-operation required to apply it. The most significant barrier identified was discolouration of the treated tooth and DPs' concern about parent and child acceptance of this. The data did however suggest that DPs believed that parents and children may be more accepting of SDF and the discolouration associated with it, when treating non-visible lesions or when used as an alternative to more invasive treatments or GA. Additional barriers such as; using SDF for managing carious lesions is an "off-label" use, the inability to claim for using SDF as it does not appear in the SDR as well as fears around fluoride safety, were also identified. DPs interviewed identified some actions that could enhance the uptake of SDF in practices. These included training courses to educate DPs about SDF use and offer reassurance about "off-label" use, and the production of information leaflets to introduce SDF to parents and children.

Research objective 3

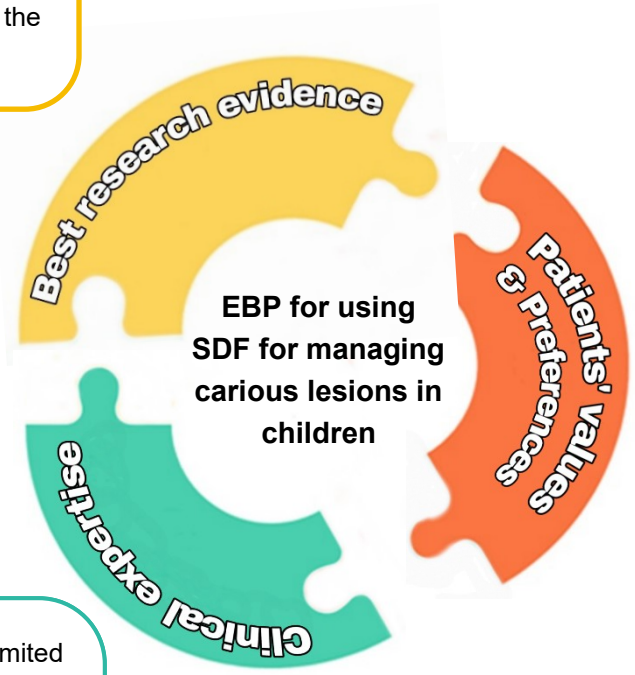
In order to address the project's third objective, exploring parents' and children's views and acceptability of SDF, a multi-method study was conducted with parents and children aged between four and twelve years old. This study investigated parents' and children's acceptability of SDF treatment, including the barriers and enablers to its use from their perspective as well as exploring their treatment preferences. This part of the study provided context to these views by exploring

the children's previous dental experience and the priorities that parents place on the management of their child's carious teeth.

Findings identified that parents believe SDF may be particularly useful for uncooperative children and the simplicity of the application procedure could make SDF an entry point to the dental environment. Concerns were however expressed in relation to the black staining effect of SDF, particularly in relation to children's front teeth. Parents suggested that this could instigate bullying at schools or nurseries and some children suggested that they would fear being picked on by their peers if they had front discoloured teeth. Both parents and children were more accepting of SDF treatment on back teeth where it is less visible. Furthermore, parents' acceptance of SDF increased if their child was apprehensive about undergoing dental treatment, with the highest levels of acceptance being associated with the avoidance of their child having a GA. It was identified that younger children appeared less self-conscious and therefore less concerned about the discolouration. Gender of the child did not seem to influence parents' decision-making process nor the child's preferences regarding the use of SDF.

Figure 6-2 summarises the EBP built for using SDF for managing carious lesions in children.

The umbrella review of systematic reviews of SDF showed that there is a consistent and progressively strengthening body of evidence that supports SDF's effectiveness for arresting coronal carious lesions in children in the primary dentition.



Parents suggested that SDF would be useful for uncooperative children. However, they and their children believed that the black staining could instigate bullying at schools. Therefore, they were more accepting of the SDF on not visible back teeth.

Parents' acceptance of SDF also increased if the child apprehensive about undergoing conventional treatment. Younger children seemed less self-conscious and less concerned about the discolouration.

Dental professionals were aware of SDF but had limited experience of using it to arrest carious lesions. They believed that the staining effect of carious lesions is a major disadvantage. They considered the application process to be simple and requires a minimum level of cooperation.
Dental professionals appreciated the potential of SDF in paediatric dentistry and suggested actions that could help overcome the barriers they highlighted.

Figure 6-2 Evidence-Based Practice for using SDF for managing carious lesions in children

Having explored DPs' views and acceptability of SDF as well as parents' and children's views and acceptability of SDF, it is clear that both groups share similar perceptions about SDF, especially in terms of its acceptability. This may be because some of the DPs interviewed for this study are also parents themselves and were considering how they would perceive SDF if it were to be used on their child.

DPs and parents independently both agreed that the main advantage of SDF was that it requires minimal child's cooperation and therefore would be advantageous for anxious and uncooperative children. The SDF application process is relatively simple and stress-free considering it only requires the use of basic tools, such as mirror, tweezers, cotton wool, petroleum jelly and a micro brush (Horst et al., 2016) and does not include a procedure that the child would find uncomfortable. Therefore, it may be helpful in introducing children to the dental environment and encourage acceptance of more complex dental treatments, this creating a more cooperative adult patient.

Both DPs and parents and children had concerns about the black staining of arrested carious lesions and how that could instigate bullying. The SDF-induced black staining has been reported thoroughly in the literature and speculated to be the one of the main barriers for using SDF in practice from parents' and children's perception (Gao et al., 2016b, Nelson et al., 2016, Duangthip et al., 2018a). In addition, it was feared that parents could be judged by others seeing their children with what appeared to be black teeth. Most studies explored parental acceptance of SDF previously had utilised questionnaire-based surveys (Crystal et al., 2017a, Alshammari et al., 2019) and even though parental concerns with the discolouration had already been reported in line with our findings , the reasons

behind these concerns were not investigated. A greater number of parents were accepting of SDF on their child's front teeth, if this was the only way to save the tooth. Few parents were reluctant to consider SDF at all. Higher parents' acceptance of SDF for the child's back teeth compared to from teeth. Previous studies explored parents' perceptions of SDF which reported similar findings (Crystal et al., 2017a, Alshammari et al., 2019, Kyoon-Achan et al., 2020).

DPs identified the metallic taste of SDF as a potential barrier however no children interviewed as part of this study complained about this. That said it should be borne in mind that a very small number of children included within this study had experience of SDF treatment. One parent commented that their child could not tolerate strange smells or tastes and therefore this may be a barrier worthy of additional exploration, especially it is thoroughly reported in the literature that SDF has an unpleasant metallic taste (Chu and Lo, 2008, Shah et al., 2014, Horst et al., 2016).

DPs suggested that having information leaflets could help introduce SDF to parents and therefore enable its use in practice. This could be advantageous regardless of parents' interest in SDF as would be raising aware of SDF, and this from the parents' perspective could also be an enabler to its use. It was suggested that as SDF becomes more popular the chance of being judged by others for the black discolouration on their children's teeth would decrease.

DPs suggested that age of the child may influence parents' decision making around the use of SDF as children often become more self-conscious with age. This idea was supported by interviewed parents who seemed more accepting of SDF for younger children (six years or younger). This was reinforced by the

interview findings from younger children. Parents showed similar attitudes in previous studies (Clemens et al., 2018, Bagher et al., 2019).

DPs believed that the gender of the child would not necessarily affect the parents' decision. Parents supported this assumption and did not consider that gender would influence their decision. Furthermore, no remarkable differences between boys' and girls' acceptability of SDF treatment were reported.

Integrating clinical expertise, patient values, and the best research evidence into the decision-making process for patient care allowed us to develop an EBP approach when it comes to the use of SDF in children. Having built this EBP picture of using SDF for managing carious lesions in children by reflecting each component through an EBP lens, decisions about choosing SDF can be based on the best current, valid and relevant evidence which was concluded from SRs retrieved by a comprehensive search in the literature. These decisions should be made by parents and children, informed by the knowledge and experience of DPs providing the treatment. However, actions are required to introduce SDF to DPs since it seemed that they have knowledge but limited experience with SDF. Parents and children's preferences should also be taken into consideration as they had some concerns about the SDF-induced black staining.

6.2 Study strengths

This study benefits from several strengths. Firstly, umbrella reviews allow information required by decision and policy makers to be more accessible and any research gaps to be identified by filtering information by systematically synthesising material from related SRs on an intervention (Smith et al., 2011,

Caird et al., 2015). Our umbrella review is the first to have systematically brought together and assessed the available SRs concerned with SDF. This allowed a more comprehensive picture to be developed using the available evidence for using SDF for managing carious lesions.

A further strength is the multi-method approach adopted. This study has employed both qualitative and quantitative methodologies which can enhance research findings, allowing the strong points of each methodology to strengthen the overall study design and produce a more complete contextual picture of the phenomenon being studied (Tariq and Woodman, 2013).

The interviews with DPs allowed the identification of new insights, some of which are applicable only for certain SDF commercial products and had not previously been reported in the literature. For example, the challenges of applying the clear liquid associated with the Riva Star product and the issue of “off-label” use of SDF for arresting carious lesions.

To the researcher’s knowledge, this study is the first, to qualitatively explore parents’ and children’s acceptance of SDF. Previous studies have explored the acceptability of SDF, focussing on parents’ views (Clemens et al., 2018, Crystal et al., 2017a, Alshammari et al., 2019, Bagher et al., 2019) and no previous studies have investigated children’s acceptability of SDF . Furthermore, this study captured younger children’s views (as young as four-years-old), an age group often neglected in research. Even though there is large body of dental research concerned with children, this has been about children rather than involving them directly (Marshman et al., 2007) because it was probably believed that data obtained from children were viewed as unreliable and invalid (Kirk, 2007). However, children can be competent participants and experts on their own

lives who can provide invaluable knowledge and unique perception (Beazley et al., 2009). There is evidence suggests that children's involvement in dental research has improved over the last decade (Marshman et al., 2015).

Finally, this is first study to have explored the use of SDF in the light of the three components of EBP.

6.3 Study limitations

There are a few caveats that should be kept in mind when interpreting the findings of this study.

In relation to umbrella review, we relied on the included SRs' findings for synthesising our results and the quality of the studies included in the SRs was not looked at. Therefore, our judgment was based on the SRs' authors appraisals of included studies within their SRs.

This study is one of the firsts to explore DPs' perceptions of using SDF for managing carious lesions in children. Purposive sampling was undertaken to ensure sample diversity. Participants were recruited through primary and secondary care from two NHS Boards. In addition, participants with varying practising experience were included. However, it should be noted that even with purposive sampling, this may not be representative of all practising DPs. Moreover, the analysis of the results relies solely on the researcher. However, to minimise the bias few interviews transcripts were double coded independently by the research and one of their supervisors. The majority of DPs interviewed for this study had no previous experience using SDF and therefore it may be that their views change as their experience grows. In addition, because SDF was only introduced into the UK in 2016 (SDI Limited, 2016), DPs who had used it before,

had limited experience and may not have had the opportunity to follow up patients over extended periods of time in order to gain a deeper understanding of the impacts on the child and family. It could be the case that with greater experience and patient follow up with patients, DPs' perceptions of the treatment may change. In addition, the interviews were conducted during the working day with busy healthcare professionals and it may be that they condensed their responses or were very focussed in their conversation due to time pressures. However, all participants completed the interview as planned and were asked if there was anything else they wished to add at the end of the interview. As a result, it is unlikely any important contributions were missed.

In relation to exploring parents' and children's acceptability of SDF, the socioeconomic level, educational level and geographical location (urban, suburban, or rural) were not explored. These factors may influence parents' acceptability of SDF. In addition, as is the case in most questionnaire studies, it remains possible that participants have provided socially desirable responses. However, participants were assured in the study's information sheet that the data were anonymised and kept confidential to minimise this social desirability bias.

6.4 Recommendations for future research

The evidence supporting SDF for preventing coronal carious lesions in children or the use of SDF in permanent teeth in children was questionable. Therefore, good-quality clinical trials investigating these outcomes are recommended.

There is no evidence around using SDF for using SDF for arresting coronal carious lesions in adults. Therefore, investigating this could be useful, especially

for exceptional circumstances where aerosol generating procedure are not recommended.

The socioeconomic level, educational level and residence location related to parents were not explored in the study. Therefore, it would be interesting to investigate if theses variables could have an impact on the level of parents' or children's acceptance of SDF.

Few children in this study had received SDF, therefore, developing a study limited to children with SDF experience could be beneficial for gathering their feedback and whether they had encountered any uncomfortable situations because of the SDF-induced black staining.

It is worthy to conduct a study comparing the effectiveness of SDF and SDF followed by KI in arresting carious lesions in addition to parents' and children's acceptance of the SDF-induced black staining of each approach.

The effectiveness of SMART restorations or SMART Hall has not been explored. Therefore, conducting studies investigating theses interventions could be worthy.

6.5 Implications for practice

The findings of this study hope to contribute to the design of implementation strategies for the use of SDF in clinical practice by informing policy makers and decision making.

It is hoped that this study will encourage the introduction of SDF into the SDR, once it has been recommended by policy makers.

The study encourages the uptake of SDF in practice as it could be one of the limited options for managing carious lesions in exceptional circumstances, such as COVID-19 pandemic where aerosol-generating procedures are not recommended (Watt, 2020).

The study suggests developing information leaflets about SDF containing the advantages, disadvantages and what outcomes to expect to help introducing this treatment to wider population. These leaflets could be disseminated to practices and Dental Hospitals across the UK.

The findings of these study advise to run CPD courses to educate DPs about SDF to familiarise them with its uses, so they become more confident with using it “off-label” for managing carious lesions.

6.6 General conclusions

Despite the well-established evidence base supporting the use of SDF for carious lesions management in primary dentition and DPs’ awareness of its use for this purpose, its uptake remains limited. Nevertheless, the potential benefits of its use were identified by both DPs and parents’ who believed that it could be particularly advantageous for less cooperative and anxious children. Barriers to its use were identified, most significantly in relation to the SDF-induced black staining, which could instigate bullying, especially for older children who may be more self-conscious.

Parents showed higher levels of acceptance for SDF for less cooperative children and in particular, as an alternative to extracting teeth under GA. Both parents and children showed a higher level of acceptance for the use of SDF on less visible back teeth, with greater opposition for its use on front teeth, especially from older

children who were worried about being picked up on at schools if they had front discoloured teeth.

Having thoroughly and systematically explored the evidence available around the use of SDF, clinical expertise with SDF and patients' values and preferences regarding the child's dental treatment, SDF is a valuable addition to the treatment options available to the paediatric dentist in caring for children with dental caries.

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PUBLICATIONS

Publication 1 Topical silver diamine fluoride for managing dental caries in children and adults

Topical silver diamine fluoride for managing dental caries in children and adults (Protocol)

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Topical silver diamine fluoride for managing dental caries in children and adults

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ABSTRACT

This is a protocol for a Cochrane Review (Intervention). The objectives are as follows:

To assess the effects of silver diamine fluoride in arresting and preventing caries in deciduous and permanent teeth (coronal and root caries) compared to any other intervention including placebo or no treatment.

BACKGROUND

Description of the condition

Dental caries is the globe's most prevalent disease (Marcenes 2013; Kassebaum 2015). Scoping reviews indicate that cost-effective preventive agents, that can be applied by families or community health workers are available, but underused (Niederman 2015). Caries affects far more than a person's oral health. The range of associated issues with untreated caries and toothaches range from reduced quality of life to poor school performance (Farber 2004; Blumenshine 2008; Seirawan 2012; Detty 2014; PR Newswire July 2015). Poor oral health is also associated with inhibited growth and development, psychosocial vulnerability, lower well-being and self-efficacy, and reduced locus of control (Quiñonez 2001; Finlayson 2007; Mattheus 2010; Adair 2013; CMS 2013).

Description of the intervention

Early studies in medicine found that silver nitrate is an effective antimicrobial agent (Von Naegeli 1893). This led to the use of silver nitrate, silver foil, and silver sutures for the prevention of ocular and surgical infections (Halstead 1895). These findings led to the application of silver nitrate to treat caries, creating sclerotic or calcified dentin formation (Stebbins 1891). The hypothesized mechanism was a potent germicidal effect combined with the de-

position of silver phosphate salt (Miller 1905; Howe 1917). Dentists termed silver nitrate 'Howe's solution' after Percy Howe, who first systematically reported on its use for caries prevention.

The specific interest in silver diamine fluoride (SDF) centers around its five presumed attributes (Thibodeau 1978): (1) control of pain and infection; (2) ease and simplicity of use (paint on); (3) affordability of material (pennies per application); (4) minimal requirement for personnel time and training (one minute, once per year); and (5) the fact that it is non-invasive. In this sense, some authors refer to SDF as a potential agent to disrupt the traditional approaches to caries prevention and control (Christensen 2009).

In vitro studies suggested that silver fluoride regimens inhibit *Streptococcus mutans* growth (Thibodeau 1978) and penetrate enamel to a depth of 25 microns, and that approximately two to three times more fluoride is retained than that delivered by sodium fluorophosphate (NaF-PO_4), sodium fluoride (NaF), or stannous fluoride (SnF_2) (Suzuki 1974). The in vitro studies suggest that the effect of SDF may be greater than that of NaF or SnF_2.

Early in vivo studies in primary teeth indicated that silver fluoride application may inhibit the lateral spread of caries (Nishino 1969). More recent, in vivo studies in permanent teeth indicated that silver fluoride may arrest approximal caries progression (Battelle 1991). These initial studies led to the use of silver diamine fluoride in Australia (Gotjamanos 1997), Japan (Yamaga 1969), and Brazil (Almeida 1994).

It is mentioned in the literature that the most effective, simplest, and least expensive caries preventive agents are silver nitrate (which kills the causative bacteria) and fluoride (which renders the teeth less soluble to bacterial acids) (Niederman 2015). The creation of a silver nitrate fluoride construct - silver diamine fluoride (SDF) - combines these two preventive agents (Rosenblatt 2009). SDF is thought to arrest and prevent decay progression by (1) killing the causative bacteria, (2) depositing a layer of protective silver phosphate that resists further decay, and (3) converting the more acid soluble hydroxyapatite to the less soluble fluorapatite (Rosenblatt 2009).

How the intervention might work

Multiple modes of action have been proposed for silver diamine fluorides (Rosenblatt 2009). This may, in part, be explained by the multiple biological organisms (e.g. bacterial, protozoan, fungal, and viral), subcellular targets (e.g. cell membranes, organelles, nuclei), and mechanisms (e.g. metabolism, replication) that have been examined. Studies indicate that silver interacts with sulfhydryl groups of proteins and with DNA, altering hydrogen bonding and inhibiting respiratory processes, DNA unwinding, cell-wall synthesis, and cell division. At the macro level, these interactions effect bacterial killing and inhibit biofilm formation (Wu 2007). The central mechanism for these diverse effects is proposed to be the interaction of silver with thiol groups (Russell 1994).

Why it is important to do this review

Several countries such as Japan, China, New Zealand, Australia, and many South American countries have been using silver diamine fluoride for many decades for arresting caries. Silver diamine fluoride is available and approved for use in multiple Asian and South American countries (Niederman 2015).

Recently in 2014 the US Food and Drug Administration (FDA) approved the use of SDF as a treatment of dentinal hypersensitivity in patients aged 21 and older, but many people have been using SDF off-label for the treatment of cavitated lesions, particularly in children. Several randomised controlled trials are showing that SDF can be used to halt the progression of caries (Rosenblatt 2009; Gao 2016).

The expanding availability of SDF and more than 100 publications cited on PubMed suggest the need for an updated systematic review examining multiple aspects of silver diamine fluoride's potential utility.

Hence, a Cochrane Review of randomised controlled trials to evaluate the effectiveness of SDF for caries arrest and prevention will provide a source of evidence for global decision making.

OBJECTIVES

To assess the effects of silver diamine fluoride in arresting and preventing caries in deciduous and permanent teeth (coronal and root caries) compared to any other intervention including placebo or no treatment.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials of parallel-group and split-mouth design comparing the use of silver diamine fluoride with any other intervention or placebo or no treatment, in patients with any type of carious lesions and without carious lesions. Any length in follow-up period will be considered for inclusion.

Types of participants

Children, adolescents and adults with any type of carious lesions or without carious lesions in anterior or posterior deciduous or permanent teeth or both.

Types of interventions

Topical application of any concentration or duration of application of silver diamine fluoride in anterior or posterior deciduous or permanent teeth with any type of carious lesions or without caries, treatment performed with or without caries excavation compared to any other intervention including placebo or no treatment.

Types of outcome measures

Primary outcomes

- Caries prevention, as measured by change from baseline in the number of decayed missing, filled permanent surfaces (DMFS), and decayed missing filled primary surfaces (dmfs).
- Caries arrest indicated by change from active to arrested caries, measured by visual changes in enamel and dentin or any other ways that may be used for caries arrest evaluation.

Secondary outcomes

- Adverse events (e.g. allergic reactions/taste disturbances, stains, decreased bond strength for direct restorations).
- Dental pain or sensitivity (e.g. pain and postoperative sensitivity may be measured by a visual analog scale (VAS), tested by practitioner or patient self-report).
- Aesthetics (e.g. acceptability of color changes in carious lesions assessed by patient, parent or clinician).

Search methods for identification of studies

Electronic searches

Cochrane Oral Health's Information Specialist will conduct systematic searches for randomised controlled trials and controlled clinical trials. Due to the Cochrane Embase Project to identify all clinical trials on the database and add them to CENTRAL, only recent months of the Embase database will be searched. Please see the searching page on the Cochrane Oral Health website for more information. No other restrictions will be placed on the language or date of publication when searching the electronic databases.

We will search the following databases for relevant trials:

- Cochrane Oral Health's Trials Register;
- the Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Register of Studies;
- MEDLINE Ovid (from 1946 onwards);
- Embase Ovid (previous six months to date).

The subject strategies for databases will be modelled on the search strategy designed for MEDLINE Ovid in Appendix 1.

Searching other resources

The following trials registries will be searched:

- US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov (http://clinicaltrials.gov/);
- World Health Organization International Clinical Trials Registry Platform (apps.who.int/trialsearch).

We will check the bibliographies of included studies and any relevant systematic reviews identified for further references to relevant trials.

We will not perform a separate search for adverse effects of interventions used for the treatment. We will consider adverse effects described in included studies only.

The search will include online abstracts indexes of conference proceedings if available such as the abstracts from the International Association for Dental Research (IADR) or the American Association of Dental Research (AADR).

Data collection and analysis

Selection of studies

For data collection and analysis two review authors (Anjana Rajendra (AR) and Analia Veitz-Keenan (AVK)) will independently and in duplicate screen the identified titles and abstracts for possible inclusion in the review. A third author (Richard Niederman (RN)) will arbitrate disagreements. We will obtain all full-text copies of all potential eligible articles and they will be further evaluated for final inclusion in detail by the review authors (AR, AVK and RN). A PRISMA flowchart will be created to summarise the process, and excluded studies will be reported.

Data extraction and management

We will create a data extraction form for the review. Four review authors independently and in duplicate will extract data. A fifth review author will moderate disagreements. All data extracted and details of all included studies will be entered in the 'Characteristics of included studies' tables using Review Manager 5 (RevMan 5) software (RevMan 2014).

For each study the following characteristics will be reported.

- Publication details (setting/year).
- Methodology.
- Type of participants.
- Type of intervention.
- Control.
- Outcomes.
- Duration and follow-up.
- Sample size.
- Funding/conflict of interest.

Assessment of risk of bias in included studies

Two review authors (AR and AVK) will independently and in duplicate assess the risk of bias for all the included randomised controlled studies by using the criteria suggested by the *Cochrane Handbook for Systematic Reviews of Interventions*, Chapter 8 (Higgins 2011). A third review author will act as a moderator for disagreements.

We will grade each study for risk of bias in the seven key domains suggested:

1. sequence generation (selection bias);
2. allocation concealment (selection bias);
3. blinding of participants and personnel (performance bias);
4. blinding of outcome assessor (detection bias);
5. completeness of outcome data (attrition bias);
6. risk of selective data reporting (reporting bias); and
7. other bias.

An overall judgment of 'Low risk' of bias for a study will be made when any plausible bias across all seven domains was unlikely to have altered the results. An overall judgment of 'Unclear risk' of bias for a study will be made when any plausible bias across one or more of the key domains raises some doubt that it may have altered the results. An overall judgment of 'High risk' of bias for a study will be made when any plausible bias across one or more of the key domains seriously weakens our confidence in the results reported in that study.

We will complete 'Risk of bias' tables for each included study. We will then generate a 'Risk of bias' summary graph and figure.

Measures of treatment effect

Caries prevention

For change in DMFT/DMFS from baseline comparing treatment groups, where studies use the same scale to measure the outcome, we will use mean values and standard deviations reported in studies to estimate the mean difference (MD) with 95% confidence intervals. For studies with different scales, we will express treatment effects as standardized mean differences (SMD) and 95% confidence intervals.

Caries arrest

Using standard 2 x 2 tables for the number of cavitated teeth arrested and non-arrested, we will express the estimate of treatment effects as odds ratios (OR) and 95% confidence intervals.

Unit of analysis issues

We are anticipating that the trials may randomise participants or teeth to the interventions. The number of observations in the analysis should match the number of 'units' that were randomised. We will follow the *Cochrane Handbook for Systematic Reviews of Interventions*, Chapter 9, Section 9.3 (Higgins 2011) in order to avoid unit of analysis errors.

Parallel trials will use standard meta-analytic procedures including standard random-effects models of pooled ORs and SMDs.

Analysis of data from split-mouth designs, where available, will be similar to that for cross-over trials (*Cochrane Handbook for Systematic Reviews of Interventions*, Section 16.4 (Higgins 2011)). For continuous outcomes, analysis will use effect estimates from paired t-tests and included in meta-analyses using the generic inverse variance method. For studies in which relevant information is not available to incorporate the published data into a meta-analysis, we will approximate paired analyses by imputing standard deviations. Specifically, we will consider borrowing standard deviation differences from similar studies. Alternatively, we will calculate standard deviation differences using a range of plausible correlation coefficients (see Sensitivity analysis). For dichotomous data we will calculate ORs for differences between groups about whether caries was arrested, along with appropriate standard errors and 95% confidence intervals, using RevMan 5 (RevMan 2014). For split-mouth studies, we will calculate ORs using the Becker-Balagtas method (BB OR) outlined in Curtin 2002 by R software Version 3.3.1 (R for Windows 3.3.1). We have chosen this method because we intend to pool data from split-mouth and parallel-group studies in the same meta-analyses, and this method is appropriate (as outlined by Stedman 2011). If an included study presented paired data by tooth pairs, we will calculate the intracluster correlation coefficient (ICC) (required for BB OR calculations) from paired data. If a split-mouth study presents data only in marginals (as parallel-group studies, not as 2 x 2 cross-classification for paired data), we will use the conservative ICC 0.05.

Dealing with missing data

We will contact authors of the selected studies for unclear methodology, missing or unclear information and missing data. For the analysis we will include only the available data. We will follow the methods suggested by Section 7.7.3 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Assessment of heterogeneity

Clinical heterogeneity will be assessed to examine the type of participants, interventions and outcomes of each study.

We will assess heterogeneity by inspection of the point estimates and confidence intervals on the forest plots. The lack of overlap of confidence intervals may indicate heterogeneity.

Statistically heterogeneity will be assessed using Cochran's test for heterogeneity and the I^2 statistic. For the interpretation of statistical heterogeneity we will use the methods outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

We will follow the guide to the interpretation of the I^2 statistic given in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011):

- 0% to 40% might not be important;
- 30% to 60% may represent moderate heterogeneity;
- 50% to 90% may represent substantial heterogeneity;
- 75% to 100% considerable heterogeneity.

For the Cochran's test for heterogeneity we will consider heterogeneity for P values < 0.1.

Assessment of reporting biases

If there are more than 10 studies included in the meta-analysis, we will test for reporting bias by testing for asymmetry in a funnel plot. If reporting biases are identified, we will carry out analysis as outlined by Egger 1997 for continuous outcomes and Rucker 2008 for dichotomous outcomes.

Data synthesis

Meta-analysis will be conducted using RevMan 5 software for studies with similar comparisons and reporting the same outcome measures. We will combine ORs for dichotomous data (caries arrest) and mean differences (caries prevention) for continuous data using random-effects models.

Outcomes from studies with different scales will be converted to standardized mean differences for continuous outcomes and overall effects will be re-scaled to a common outcome type.

We will perform meta-analysis if appropriate in order to obtain a pooled relative risk (OR) for dichotomous outcomes, mean differences and standardized mean differences (SMD) for continuous outcomes to assess the effect of topical silver diamine fluoride in control of dental caries.

Subgroup analysis and investigation of heterogeneity

As described above, subgroup analysis will be considered for any outcome with an estimated I^2 of 40% to 60%, considered as possible moderate heterogeneity according to the *Cochrane Handbook for Systematic Reviews of Interventions*, Section 9.5.2 (Higgins 2011). However, prior to any subgroup analyses we will consider both magnitude and direction of effects and strength of the evidence for heterogeneity, via confidence intervals for the I^2 statistic. Subgroup analysis will be performed for study design and by predominant age group in the study.

Sensitivity analysis

Provided there are sufficient included trials we will conduct sensitivity analysis to evaluate the impact of the following factors:

- studies of high and unclear risk of bias;
- for split-mouth designs, sensitivity analyses will be conducted to assess the impact of variation in imputed correlations for the calculation of standard deviations of differences and odds ratios.

Presentation of main results

The primary and secondary outcomes will be included in 'Summary of findings' tables using GRADEpro software (GRADEpro GDT 2014). We will assess the quality of the body of evidence with reference to the overall risk of bias of the included studies, inconsistency and directness of the evidence, the precision of the estimates, and the publications bias.

We will categorize the quality of the body of evidence for each outcome as high, moderate, low and very low.

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* *Indicates the major publication for the study*

APPENDICES

Appendix 1. MEDLINE Ovid search strategy

1. exp Tooth demineralization/
2. (teeth adj5 (cavit$ or caries or carious or decay$ or lesion$ or demineral$ or remineral$)).mp.
3. (tooth adj5 (cavit$ or caries or carious or decay$ or lesion$ or demineral$ or remineral$)).mp.
4. (dental adj5 (cavit$ or caries or carious or decay$ or lesion$ or demineral$ or remineral$)).mp.
5. (enamel adj5 (cavit$ or caries or carious or decay$ or lesion$ or demineral$ or remineral$)).mp.
6. (dentin adj5 (cavit$ or caries or carious or decay$ or lesion$ or demineral$ or remineral$)).mp.
7. (root adj5 (cavit$ or caries or carious or decay$ or lesion$ or demineral$ or remineral$)).mp.
8. Dental plaque/
9. ((dental or tooth or teeth) and plaque).mp.
10. or/1-9
11. (silver adj3 fluorid$).mp.
12. ("silver diamine" or "diamine silver" or "silver diammine" or "diammine silver").mp.
13. ((silver adj nitrate) or (silver adj3 protein$) or (nano adj3 silver)).mp.
14. ((ammonical or ammoniacal) adj2 silver).mp.
15. (SDF or AgF or AgNO3 or Ag-nano).ti,ab.

16. ("Advantage Arrest" or "Howe?s Solution" or "Riva Star" or Cariestop or Ancarie or "Salfluoraide di Walter" or (Cariostatic adj4 Inodon) or Saforide or Flurophat or Fagamin or Bioride).mp.
17. or/11-16
18. 10 and 17

CONTRIBUTIONS OF AUTHORS

All authors were responsible for writing and drafting the protocol.

DECLARATIONS OF INTEREST

Anjana Rajendra: no interests to declare.

Analia Veitz-Keenan: no interests to declare.

Branca Heloisa Oliveira: no interests to declare.

Ryan R Ruff: no interests to declare.

May CM Wong: no interests to declare.

Nicola PT Innes: no interests to declare.

John Radford: no interests to declare.

Nassar Seifo: no interests to declare.

Richard Niederman: has several articles on silver diamine fluoride and grants submitted to examine silver diamine fluoride's comparative effectiveness.

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RESEARCH ARTICLE Open Access

Silver diamine fluoride for managing carious lesions: an umbrella review

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Abstract

Background: This umbrella review comprehensively appraised evidence for silver diamine fluoride (SDF) to arrest and prevent root and coronal caries by summarizing systematic reviews. Adverse events were explored.

Methods: Following Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines, PubMed, Embase, Cochrane Library, PROSPERO register and Joanna Briggs Institute Database of Systematic Reviews were searched for systematic reviews investigating SDF for caries prevention or arrest (1970–2018) without language restrictions. Systematic reviews were selected, data extracted, and risk of bias assessed using ROBIS by two independent reviewers, in duplicate. Corrected covered area was calculated to quantify studies' overlap across reviews.

Results: Eleven systematic reviews were included; four focussing on SDF for root caries in adults and seven on coronal caries in children. These cited 30 studies (4 root caries; 26 coronal caries) appearing 63 times. Five systematic reviews were of "low", one "unclear" and five "high" risk of bias. Overlap of studies was very high (50% root caries; 17% coronal caries). High overlap and heterogeneity, mainly comparators and outcome measures, precluded meta-analysis. Results were grouped by aim and outcomes to present an overview of direction and magnitude of effect. SDF had a positive effect on prevention and arrest of coronal and root caries, consistently outperforming comparators (fluoride varnish, Atraumatic Restorative Treatment, placebo). For root caries prevention, the prevented fraction (PF) was 25–71% higher for SDF compared to placebo (two systematic reviews with three studies) and PF = 100–725% for root caries arrest (one systematic review with two studies). For coronal caries prevention, PF = 70–78% (two systematic reviews with two studies) and PF = 55–96% for coronal caries arrest (one systematic review with two studies) with arrest rates of 65–91% (four systematic reviews with six studies). Eight systematic reviews reported adverse events, seven of which reported arrested lesions black staining.

Conclusion: Systematic reviews consistently supported SDF's effectiveness for arresting coronal caries in the primary dentition and arresting and preventing root caries in older adults for all comparators. There is insufficient evidence to draw conclusions on SDF for prevention in primary teeth and prevention and arrest in permanent teeth in children. No serious adverse events were reported.

Keywords: Silver diamine fluoride, Systematic review, Overview, Umbrella review

Background

Dental caries continues to be one of the most prevalent chronic diseases in the world, affecting people across all age groups and countries [1]. Carious lesions can be both prevented and arrested using fluoride-based materials such as professional applied varnishes [2, 3]. Silver diamine fluoride (SDF) was cleared by the Food and Drug Administration in the United States in 2014 [4] with growing interest in its use supported by reports of its effectiveness [5–7]. Silver and fluoride in an alkaline solution act synergistically to arrest carious lesions through a variety of mechanisms [8].

By assessing studies, systematic reviews have explored SDF's effectiveness to prevent and arrest carious lesions. The ideal systematic review on which to base a clinical decision or guideline would be externally and internally valid, use high-quality methodology, comprehensively include all evidence and carry out a meta-analysis [9]. However, there is no single systematic review of obvious higher quality and recency that should be prioritised in

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decision-making by those considering adding SDF to their clinical treatment options for patients.

Umbrella reviews also known as systematic reviews of systematic reviews, or overview of systematic reviews, are a relatively new methodology [10, 11]. They filter information by systematically synthesising material from related systematic reviews of an intervention for multiple outcomes. This type of data synthesis allows information required by decision and policy makers to be more accessible and any research gaps to be are identified [12–14]. We have taken an approach, using the Joanna Briggs Institute methodology [15], Cochrane guidance (Becker and Oxman [17]) and recommendations from a recent Cochrane symposium [16], to conduct a transparent review of systematic reviews of SDF.

This umbrella review aimed to provide a low-bias, comprehensive assessment on what the evidence from systematic reviews tells us about using SDF for management of carious lesions in children and adults.

Objectives

To assess systematic reviews, with or without meta-analyses, of SDF's effectiveness for:

1- The breadth of evidence assessed in the systematic reviews (systematic reviews' characteristics and characteristics of their included studies);
2- The risk of bias of the systematic reviews;
3- The arrest and prevention of root and coronal carious lesions in primary and permanent teeth;
4- Adverse events and side effects associated with SDF application.

Methodology

The protocol was registered in PROSPERO (CRD42 017070063) and followed Joanna Briggs Institute [15] and Cochrane methodology [16, 17].

Inclusion criteria

Systematic reviews with/without meta-analysis investigating SDF (any concentration and frequency) compared with active comparators, placebo and no treatment, for arresting or preventing coronal or root carious lesions in children and adults with or without carious lesions in primary and/or permanent teeth.

Exclusion criteria

Primary studies investigating SDF or reviews that did not meet the definition of systematic reviews i.e. included a thorough plan and search strategy developed in advance; and aimed to minimise bias by including, appraising, and synthesizing all relevant studies [18].

Databases and search strategy

We searched databased that contained systematic reviews of health interventions: PubMed, Embase, Cochrane Database of Systematic Reviews and Joanna Briggs Institute Database of Systematic Reviews and Implementation Reports. We also searched the PROSPERO database to allow identification of any forthcoming systematic reviews. These were all searched between 1970 (when SDF was first investigated) and June 2018.

Searches were built around the key words: "silver diamine fluoride" OR "silver diammine fluoride" OR "diamine silver fluoride" OR "diammine silver fluoride" OR "silver fluoride" AND "caries" OR "carious" OR "decayed" OR "cavity" (Additional file 1). AND "review" OR "meta-analysis" was included for databases without a predefined search filter for review articles. No additional search for primary studies was conducted. No language restrictions were applied. Bibliographies of retrieved papers were manually screened to identify additional potential reviews for inclusion.

Reviews selection process

The search results were imported to Endnote, and duplicates removed. Titles/abstracts screening was performed independently and in duplicate by two reviewers. Full texts of publications considered potentially eligible were retrieved and assessed independently and in duplicate. Where there were discrepancies, a third reviewer was consulted, with discussion until agreement.

Data collection and synthesis

A standardised data extraction tool was developed a priori and refined based on pilot testing. The data extracted included specific details, such us search strategy, PICO items, objectives, number of included studies (Additional files 2A/B and 3A/B). Two independent reviewers extracted data in duplicate. Root caries systematic reviews and coronal caries systematic reviews were analysed separately because their target populations were different with root caries studies focused on older adults and coronal caries studies on children, and they included different studies with no overlapping included studies. For systematic reviews investigating other interventions alongside SDF, only SDF data were considered.

The breadth of evidence and adverse events assessed in the systematic reviews were summarised narratively through data tables of the review characteristics. To analyse the effectiveness of SDF for managing carious lesions, synthesis of similar outcome measures would have had to be carried out to compare these across comparator interventions and where possible meta-analyses would be carried out.

Analysis of the degree of overlap in studies

To determine the overlap in studies across the systematic reviews, citation matrices were generated and "Corrected Covered Areas" (CCAs) were calculated (Fig. 1). CCA = 0–5; slight, 6–10; moderate, 11–15; high, and > 15; very high overlap [19].

Reviews' risk of bias

Two reviewers assessed risk of bias within systematic reviews independently and in duplicate using Risk of Bias in Systematic reviews (ROBIS) [20]. This assesses the systematic reviews across three areas; 1) relevance of the review, 2) identifying concerns within the systematic review process under four domains; study eligibility criteria, identification and selection of studies, data collection and study appraisal, and synthesis and findings and 3) judging risk of bias. These are then considered together to give a "low", "high" or "unclear" risk of bias score. Scoring discrepancies were resolved through discussion until consensus was reached. Authors were contacted where clarification was required.

Results

Figure 2 shows the flow of reviews through searching and assessing. The initial searches yielded 41 potential reviews. Twelve duplicates were removed, and four additional publications added from screening bibliographies resulting in 33 potentially eligible reviews. Following title and abstract screening, 14 papers were excluded and a further eight [3, 4, 21, 23, 25–28] after assessing full texts. Therefore, 11 systematic reviews were included, reporting on 63 studies in total, 30 out of which, were unique.

Breadth and comprehensiveness of the evidence

Four systematic reviews focussed on root caries [24, 29–31] and seven on coronal caries [5, 22, 32–36]. They included 30 studies (4 root caries; 26 coronal caries). Characteristics of the systematic reviews and studies are summarised below. See Additional files 2A/B, 3A/B and 4 for further details.

Characteristics of the reviews

Most systematic reviews covered a defined timeframe, ranging from 1946 to 2017. However, one narrowed it to 2005 to 2015 [33]. PubMed, Cochrane Library and Embase databases were searched most frequently. One systematic review explored grey literature, dissertations and theses [32]. Two systematic reviews searched for on-going trials, dissertations and theses [31, 35]. Only three systematic reviews did not impose any language restrictions [31, 32, 35]. Five systematic reviews restricted language to English [5, 29, 30, 33, 34]. One included English, Spanish and Portuguese [36], one included English and German [24] and one included Japanese, Chinese, English, Portuguese and Spanish [22].

Six systematic reviews considered only children [5, 22, 32–35], whereas, one did not specify an age group indicating "humans" [36]. These seven focused on coronal caries. Two systematic reviews included older adults [29, 30] while two specified adults with exposed root surface [24, 31]. These four systematic reviews focussed on root caries.

Seven systematic reviews included studies investigating SDF alone rather than other interventions [22, 30–33, 35, 36] and four investigated additional agents [5, 24, 29, 34]. Six systematic reviews did not specify a comparison to the intervention [5, 22, 29, 30, 33, 34]. Three systematic reviews included studies comparing the intervention to no treatment, placebo or other interventions [24, 31, 32, 35]. One systematic review compared SDF to fluoride varnish [36].

Seven systematic reviews investigated the effect of SDF on coronal carious lesions with four focussing on lesions arrest [5, 22, 32, 34], one on prevention only [35] and two on both prevention and arrest [33, 36]. Of the four systematic reviews that investigated root caries, one focused on carious lesions prevention only [29], three explored carious lesions prevention and arrest [24, 30, 31]. Eight systematic reviews reported adverse events and side effects associated with SDF treatment [5, 22, 30, 31, 33–36].

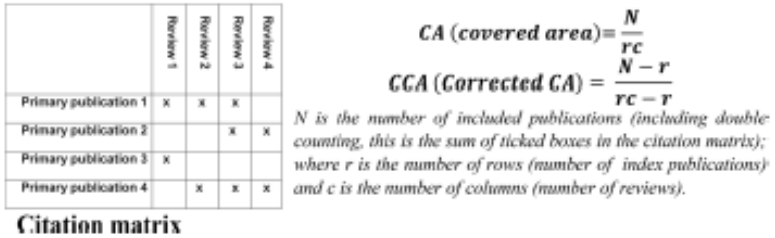

Fig. 1 Citation matrix and calculation formulae. CA, covered area; CCA, corrected covered area. 0–5 = slight; 6–10 = moderate; 11–15 = high; over 15 = very high. (Reproduced with the author's permission) [19]

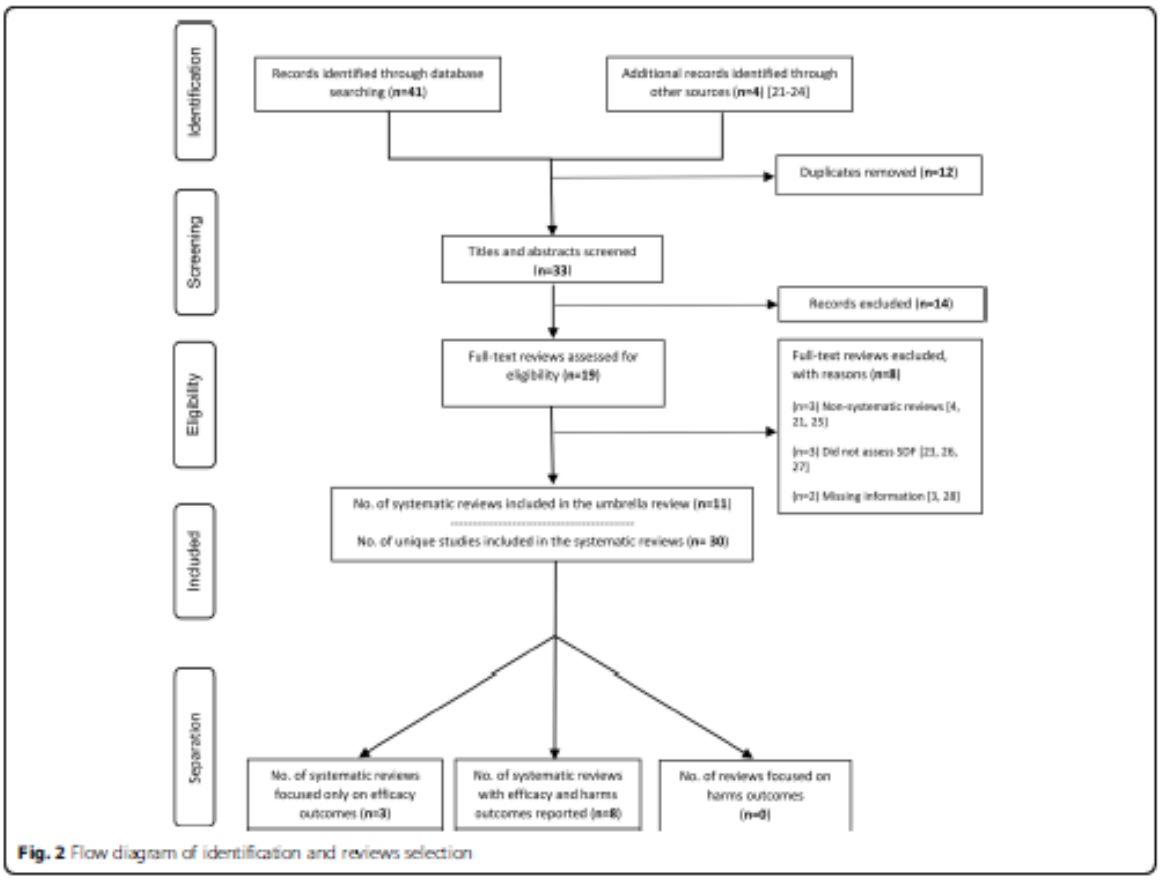

Fig. 2 Flow diagram of identification and reviews selection

The systematic reviews used six different outcome measures: % success rates [5, 22, 29, 34]; prevented fraction (PF) [30, 31, 35, 36]; number needed to treat (NNT) [30, 36]; weighted mean difference (WMD) [31, 35]; mean difference (MD) [24] and risk ratio (RR) [32]. The outcome measurement was not clear in one systematic review that did not synthesise results from included studies but presented the original reported data [33]. Six conducted meta-analyses to synthesize the findings [22, 24, 31, 32, 34, 35].

Eight systematic reviews used Cochrane risk of bias assessment tool or a simplified version based on its recommendations [5, 22, 24, 31–35]. One used Jadad,1998 [36], and one used the critical appraisal sheet for randomized controlled trials (RCTs) from Oxford Centre for Evidence-Based Medicine [30]. However, one systematic review did not evaluate the included studies [29]. Regarding grading the quality of evidence, two systematic reviews used GRADE [24, 32].

Characteristics of the studies included in the reviews

The number of studies contained within the systematic reviews varied widely; three systematic reviews included one or two RCTs [24, 29, 36], while others included seven or more. Gao included seven RCTs focussing on SDF in one systematic review [34] and 19 prospective clinical trials in another [22].

Five systematic reviews did not state the studies' country of origin [24, 29, 32, 34, 36]. Eight studies were conducted in Brazil, seven in Hong Kong, six in China and four in Japan. One study was conducted in each of the following countries: Nepal, Philippines, Cuba, Argentina and Turkey.

The first trial investigating SDF was published in 1969 [37]. Despite all systematic reviews apart from one systematic review [33] searching earlier timeframes, only one retrieved studies published before 2002 [22].

The root caries studies were of high quality and at low risk of bias, while for coronal caries studies; the reliability of those conducted before 2002 was relatively low, while studies after that were of better quality.

Systematic reviews' risk of bias

Five systematic reviews were at high [5, 24, 29, 30, 36], five were at low [22, 31, 32, 34, 35] and one was at unclear [33] risk of bias (Additional file 3A/B).

As SDF is popular in non-English speaking countries and studies were often reported in non-English journals, limiting to English language reduced the comprehensiveness of included studies and immediately placed significant bias within those systematic reviews [5, 29, 30, 33, 34]. In addition, the absence of a priori designed protocol, affected the risk of bias score for eight systematic reviews since there was no indication that predefined analyses were followed [5, 22, 24, 29, 30, 33, 34, 36].

Three systematic reviews did not report whether study selection had been undertaken independently and in duplicate [30, 33]. Moreover, two did not report whether bibliography screening or other manual search methods were used [5, 33].

It was unclear in three systematic reviews whether data collection had been undertaken, independently and in duplicate [30, 33, 34]. All systematic reviews, except one which did not appraise the included studies [29], appraised the studies using appropriate criteria.

Findings of the reviews

In umbrella reviews, the role of the reviewer is to appraise the evidence from the systematic reviews and not the studies. The appropriateness of re-analysis of studies' data has been debated but it is generally agreed that where novel analyses are the aim, a review of studies should be undertaken rather than an overview of reviews [13, 38]. systematic reviews outcome and outcome measures heterogeneity meant that meta-analysis was not appropriate. However, we combined systematic review results together to present an overview of direction and magnitude of effect where there was the same outcome measure [39]. (Additional files 3A/B and 4).

Root carious lesions management in adults

For root carious lesions prevention and arrest, all four systematic reviews compared SDF to placebo and found the direction of effect favoured SDF i.e. there were more prevented and arrested lesions with the use of SDF.

Carious lesions prevention For root carious lesions prevention, the success rates were 72% higher for 38% SDF compared to placebo based on one high risk of bias systematic review including one study [29]. The MD for changes in DMFRS/DFRS was − 0.33 (95% CI = − 0.39, − 0.28) for 38% SDF compared to placebo based on one high risk of bias systematic review with meta-analysis of two studies [24]. The PF was 25–71% for 38% SDF compared to placebo based on one low [31] and one high [30] risk of bias systematic reviews including four studies.

Carious lesions arrest For root carious lesions arrest the PF was 100 to 725% higher for 38% SDF than placebo based on a single high risk of bias systematic review [30] with data from two studies. One low risk of bias systematic review reported that 38% SDF was significantly more effective than placebo in arresting root carious lesions (pooled results were not calculated) [31]. One systematic review found that SDF can be efficacious to decrease progression of root carious lesions (no numeric results reported) [24].

Coronal carious lesions management in children

For coronal carious lesions prevention and arrest, all seven systematic reviews focused mainly on primary dentition and all reported that SDF outperformed the comparators regardless of the outcome measure.

Carious lesions prevention Coronal carious lesions prevention was reported in three systematic reviews; one at low risk of bias focused only on the primary dentition [35] and one at unclear [33] and one at high [36] risk of bias focused on the primary dentition and first permanent molars. The PF for 38% SDF compared to placebo ranged from 70 to 78% in the primary dentition based on two systematic reviews [35, 36] including two studies and was 64% in the permanent first molars based on one systematic review [36] with one study [6].

For fluoride varnish compared to placebo in the primary dentition the PF was 54% based on one systematic review [35] with one study [40]. The same systematic review reported that glass ionomer cement was more effective than 30% SDF at 12 months, PF = − 6%, but the difference was not statistically significant.

One systematic review presented studies' original results and concluded that SDF showed potential as a caries preventive treatment in the primary dentition and for first permanent molars [33].

Carious lesions arrest Coronal carious lesions arrest was reported in six systematic reviews; three at low [22, 32, 34], two at unclear [33] and one at high [5, 36] risk of bias systematic reviews including eight studies.

The reported 38% SDF arrest rates in the primary dentition ranged from 65 to 91% based on three systematic reviews [5, 22, 34]. These were 38 to 44% for fluoride varnish, 39 to 82% for glass ionomer cement, and 34% for placebo. The PF based on one systematic review [36] with two studies ranged from 55 to 96% in favour of 38% SDF when compared to fluoride varnish or placebo in primary dentition. However, this was 100% for permanent first molars based on one study [6]. The RRs were 1.66 for SDF compared to fluoride varnish or Atraumatic Restorative Treatment and 2.54 compared with placebo/no treatment based on one systematic review which focused only on the primary dentition [32] and including two studies. One systematic review

presented the studies' original results and concluded that SDF at concentrations of 30 and 38% is more effective than other strategies in arresting coronal carious lesions in primary dentition [33].

Adverse events and side effects Eight systematic reviews reported adverse events and side effects associated with SDF [5, 22, 30, 31, 33–36]. The main side effect reported was black staining of the carious lesions although older adults rarely complained about that. Similarly, the discoloration was acceptable in children, concerning 7% of participants in one study [40].

Adverse events were classified into two categories according to the FDA definition and classification of adverse events [41]; suspected adverse reaction or adverse event where there is a reasonable possibility that this is caused by the drug, and serious adverse event or serious suspected adverse reaction. An adverse event is considered "serious" if it causes death, a life-threatening event or in-patient hospitalisation.

Regarding suspected adverse reactions, reversible, small, mildly painful white lesions in oral mucosa, due to inadvertent contact with SDF, were reported; these healed uneventfully within 48 h. There was no difference in pulpal irritation incidence between the control and experimental groups. A metallic taste or burning sensation was not reported in any of the studies. No serious adverse events, such as allergic reactions or toxicity were reported.

Discussion

We identified 11 systematic reviews (of 30 studies) investigating SDF for carious lesions prevention and/or arrest; seven focused on coronal caries in children, and four on root caries in adults. This is a high ratio of studies to systematic reviews with several published in the last few years indicating that no single systematic review seems to have incorporated all the evidence and comprehensively covered the topic. We have attempted to address this by systematically appraised the evidence from the systematic reviews using a transparent methodology and have found that all systematic reviews, despite variability in methodology, found SDF to be more effective for carious lesions prevention and arrest than any of the comparators.

When interpreting the results of this umbrella review, it should be kept in mind that the individual studies included in the systematic reviews are not scrutinised. Therefore, our conclusions rely on the interpretation of the systematic reviews' authors. This is in line with the accepted umbrella review methodology and capitalises on the fact the original studies had their qualities appraised within the systematic review in which they were reported.

With 11 systematic reviews including 30 studies and within this, four systematic reviews focussing on root caries including four studies, the overlap in studies across systematic reviews was very high in both matrices [19]. The CCA was 0.5 for root caries systematic reviews (50% overlap) and 0.17 for coronal caries systematic reviews (17% overlap) (Figs. 3 and 4). This means that a large number of studies appeared several times across the systematic reviews. Consequently, repeated studies would have had unintentionally stronger weighting in any meta-analyses. This, together with heterogeneity of comparators and outcome measures limited synthesis of the results and precluded meta-analyses. In addition, in line with standard Umbrella review methodology, each meta-analysis was not re-calculated to confirm validity. However, allowing for these caveats, this umbrella review is the first such review systematically summarising the current evidence for the effectiveness of SDF for carious lesions prevention and arrest. It followed a systematic approach that included a comprehensive search strategy of five databases with independent, duplicate systematic review selection and data extraction and an accepted method to assess risk of bias.

Many SDF studies have been set in non-English speaking countries such as China and Brazil. Thirteen out of the 30 unique studies were published in non-English languages. However, five systematic reviews excluded non-English studies, and this is likely to have introduced bias into their dataset, analyses and conclusions.

There was wide variability in the number of included studies ranging from only two [36] up to 19 [22] even when they investigated similar interventions/comparators, aims and outcomes as well as including similar study designs. Without further investigation, it was not possible to determine the reason for this, however there is an interesting difference between the coronal and root caries systematic reviews. In the root caries systematic reviews, Fig. 3 shows that when the systematic review was more recent, there were more studies included, and all seem to have been captured by the searches. This

	Systematic reviews			
Primary studies	Gluzman et al., 2013	Wierichs et al., 2015	Hendre et al., 2017	Oliveira et al., 2018a
Tan et al., 2010	X	X	X	X
Zhang et al., 2013		X	X	X
Li et al ,2016			X	X
Li et al ,2017				X

Fig. 3 Citation matrix for reviews assessed the effectiveness of SDF for root carious lesions management

	Systematic reviews						
Primary studies	Rosenblatt et al., 2009	Duangthip et al., 2015	Gao et al., 2016a	Gao et al., 2016b	Contreras et al., 2017	Chibinski et al., 2017	Oliveira et al., 2018b
Nishino et al., 1969			X				
Yoshida et al., 1976			X				
Tsutsumi et al., 1981			X				
Wang, 1984			X				
Oliveira, 1985			X				
Maciel, 1988			X				
Bijella, 1991							X
Ye, 1995			X				
Miasato, 1996			X				
Fukumoto et al., 1997			X				
Lo et al., 2001				X			
Yang et al., 2002			X				
Chu et al., 2002	X	X	X	X		X	X
Mauro et al., 2004			X				
Llodra et al., 2005	X		X	X	X	X	X
Huang et al., 2006			X				
Braga et al., 2009			X	X	X		
Yee et al., 2009			X	X	X	X	
Vasconcelos, 2011						X	
Monse et al., 2012					X	X	
Liu et al., 2012						X	
Zhi et al., 2012		X	X	X	X	X	X
dos Santos et al., 2012		X	X	X	X	X	
Seberol and Okte, 2013						X	
Dos santos et al., 2014						X	
Duangthip et al., 2016			X		X	X	

Fig. 4 Citation matrix for reviews assessed the effectiveness of SDF for coronal carious lesions management

contrasts with Fig. 4 which shows an irregular pattern of study inclusion for the coronal caries systematic reviews. This pattern is not explained by the search timeframe or year of publication as more recent systematic reviews would be expected to include more recently published studies in addition to capturing all previous ones. Although it was not within the remit of this review to undertake a full exploration of the reasons for inclusion and exclusion of studies in the systematic reviews, it does not seem to be explained by differing inclusion/ exclusion criteria or other methodological decisions. Some of these findings might offer insight into this and inform future work looking at the quality of systematic reviews. For example, one study [42] investigated the effectiveness of Nano Silver Fluoride (NSF) for preventing and arresting carious lesions in children. It was included in a review investigating SDF [32] and the justification given, on contacting the authors, was because NSF contained the same components as SDF; this effect remained the same even when silver fluoride was chemically treated to obtain nanoparticles of silver. However, other investigators excluded this study, possibly because they viewed NSF as different from SDF. Alternatively, they did not detect this paper in their search. On the other hand, the same systematic review [32] excluded a study [43] investigating SDF in arresting occlusal carious lesions in first

permanent molars because the method of evaluation was based on qualitative scores. However, it was included in three other systematic reviews [22, 33, 34]. Although this finding is incidental and was not one of the aims of the umbrella review, it is notable and perhaps worth investigating further. It is not possible to quantify this in terms of quality of the individual reviews and this is perhaps a limitation of umbrella reviews. The usefulness of the risk of bias scoring tools is also questioned with these findings. If one of these systematic reviews was assessed individually, it could score at low risk of bias and be considered as a good systematic review for basing policy on, yet there could be many studies not included and a resulting hidden high risk of bias with no insight into the consequences of omitting certain studies. Poor decisions to include or exclude studies could easily go undetected. The lack of comprehensiveness in the systematic reviews is not fully related to low quality and only revealed by comparing the systematic reviews.

These findings highlight the need for meticulous attention to be paid during studies' selection processes and for those appraising reviews to be aware that this might be a shortcoming not detected during quality appraisal. It also stresses the need for systematic reviews to provide data justifying the exclusion of each study, and not simply report the total number of excluded studies with overall reasons. This would help clarify whether all possible studies were found through searching and rule out selection bias. So, even systematic reviews at low risk of bias, according to ROBIS tool, might fail to provide healthcare decision makers with accurate evidence depending on how they include or exclude studies relevant to their question. For SDF, all the systematic reviews pointed to evidence of a positive effect rather than conflicting results depending on which systematic review was looked at.

For the root caries systematic reviews, the main limitation was around conclusions being based on a limited number of included studies (one systematic review drew conclusion based on only one study). This demonstrates the need for more well-conducted RCTs investigating SDF for root carious lesions management. Imposing language restrictions and the absence of a priori designed protocol had affected the risk of bias in three out of the four systematic reviews. One systematic review brought dentine hypersensitivity into their conclusions even though this was neither included in the search nor discussed through the systematic review [30].

For the coronal caries systematic reviews, a larger number of studies was included in the systematic reviews. However, the quality of included studies varied with those conducted before 2002 being of low reliability. Moreover, the methodology and outcome measurements varied between studies which made combining the results challenging. This supports the need for designing a standardised methodology and following a core outcome set, if possible, for studies in reporting their results, in order to enable systematic reviews in synthesising the evidence from all available relevant studies.

Further details about the limitations of each included systematic review can be found in Additional file 3A/B.

Another finding worth noting was that the search in the PROSPERO register retrieved six ongoing, apparently unfinished systematic reviews. Three were completed and published however their statuses had not been updated in PROSPERO [31, 32, 35]. It was possible however to retrieve these from searches in PubMed and Embase.

Overall, all systematic reviews reported that SDF was effective in managing carious lesions. However, earlier ones tended to overstate conclusions around SDF's effectiveness given the limited number of trials they were based on, and the systematic reviews' high risk of bias. More recent systematic reviews reported increasing numbers of trials and were of lower risk of bias.

For root carious lesions *prevention and arrest*, the systematic reviews were based on only four clinical trials. However, all trials were assessed as high quality in the systematic reviews.

There was a large variability in the number of studies included in the coronal caries systematic reviews and the reasons for this were unclear.

For coronal carious lesions *prevention*, it is noteworthy that the number and quality of studies included in the systematic reviews was low which questions the evidence base around SDF for coronal carious lesions prevention.

For coronal carious lesions *arrest*, an increased number of systematic reviews have reported stronger evidence to support SDF use in the primary dentition. There is insufficient evidence to draw conclusions for its use in permanent teeth in children as there are so few studies.

Conclusions

Although there are not a large number of clinical trials, there is a consistent and progressively strengthening body of research that supports SDF's effectiveness for arresting coronal carious lesions in children in the primary dentition and arresting and preventing root carious lesions in older adults. However, the evidence base around SDF for preventing coronal carious lesions in children was questionable based on the number and quality of studies. Moreover, there are too few studies and insufficient evidence to draw conclusions on the use of SDF in permanent teeth in children.

Additional files

Additional file 1: PubMed search strategy. (DOCX 22 kb)

Additional file 2: Root and coronal caries reviews characteristics. (DOCX 47 kb)

Additional file 3: Root and coronal caries reviews' findings and quality appraisal. (DOCX 168 kb)

Additional file 4: Characteristics of reviews related to outcomes, outcome measures and results. (DOCX 40 kb)

Abbreviations

CCA: Corrected covered area; FDA: Food and Drug Administration; MD: Mean difference; NNT: Number needed to treat; NSF: Nano silver fluoride; PF: Prevented fraction; RR: Risk ratio; SDF: Silver diamine fluoride; WMD: Weighted mean difference

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Not applicable.

Authors' contributions

NS and NI conceived of the project. NS, HC, JR and NI wrote the protocol, carried out the systematic review, prepared and approved the manuscript.

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Availability of data and materials

The authors declare that the data supporting the findings of this study are available within the article and its supplementary information files.

Ethics approval and consent to participate

Not applicable as this work is a data synthesis of existing systematic reviews in the literature and has involved no individuals, requiring no consent to participate.

Consent for publication

Not applicable as there are no data, pictures or illustrations relating to individuals that require consent to publish.

Competing interests

The authors declare that they have no competing interests.

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Publisher's Note

Publication 3 The use of silver diamine fluoride (SDF) in dental practice

VERIFIABLE CPD PAPER
Caries

CLINICAL

The use of silver diamine fluoride (SDF) in dental practice

Nassar Seifo,[1] Mark Robertson,[1] Jeanette MacLean,[2] Katharine Blain,[3] Sarah Grosse,[3] Roderick Milne,[1] Clement Seeballuck[1] and Nicola Innes*[1]

Key points

- Explains why, how and when clinicians should use SDF.
- SDF is currently not licenced for caries arrest. This article explains what this means for clinicians and how they should approach this issue
- Explains the side-effects and potential adverse events associated with SDF use and how to manage these

Abstract

Silver diamine fluoride (SDF) is a clear, odourless liquid indicated for desensitisation of non-carious tooth lesions and molar incisor hypomineralisation. It is also useful for arresting carious lesions in adults and children who are high caries-risk and/or have difficult-to-control, progressing carious lesions, those who are unable to tolerate invasive treatment, elderly populations, and those who are medically compromised or have additional care and support needs. SDF may be used to manage lesions that are too extensive to restore but not associated with pain and/or infection. This can be important particularly where extractions might be contra-indicated for medical or behavioural reasons. This paper summarises the global evidence for the effectiveness and safety of SDF, describes what it is, its mechanisms of action and presents recommendations on how to use it. There are details on indications/contra-indications and risks/benefits to be considered in the use of SDF also discussion of how to approach SDF's side effect of black staining of carious tooth tissue. We give an example of an information sheet (Appendix S1, see online supplementary information) that may be used when discussing SDF with patients, particularly for primary teeth in children, but adaptable for the permanent dentition and for adults.

Introduction

Dental caries and silver diamine fluoride (SDF) – a brief introduction

In 1900, GV Black observed that 'Caries of the teeth is the most prevalent disease to which man is liable. There is no other disease which afflicts so large a proportion of the human family.'[1] Over one hundred years later, it may seem that not much has changed, with untreated dental caries in permanent teeth being the most prevalent condition of humankind, affecting 2.5 billion people worldwide.[2] Cariology research has improved understanding of the pathological process involved in the initiation and progression of the disease, and of the efficacy and effectiveness of strategies to manage caries and its consequences. This includes supporting the use of cariostatic agents to stop the progress of the disease as part of treatment, rather than limiting the focus of treatment to restorative options alone.[3] Minimal intervention dentistry (MID)[4] as a concept within oral healthcare was once considered a peripheral and unconventional topic but has now moved to centre-stage of oral health care. MID embodies a patient-centred approach to care, is evidence-based and supports development of novel treatment options. One of these is silver diamine fluoride (SDF) as a cariostatic agent. SDF was first recorded as being used in Japan in 1969 but has recently had a renaissance.[5]

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What is silver diamine fluoride (SDF)?

SDF is a colourless, odourless solution of silver, fluoride and ammonium ions, the ammonia acting as a stabilising agent for the solution. It looks just like water, although one product, Advantage Arrest (Elevate Oral Care, Florida), not available in the UK, is tinted blue. SDF (38%) contains a high concentration of fluoride ions; 44,800 ppm. When placed on carious tooth tissue, a series of chemical reactions take place that promote tooth desensitisation by dentinal tubule blockage and carious lesion arrest by dentinal tubule blockage, bacterial death, remineralisation of demineralised tooth and inhibition of dentinal collagen degradation (Fig. 1). These chemical reactions have the side effect of staining carious lesions (enamel and dentinal) permanently black (Fig. 2) but sound enamel does not stain.[6] It is therefore also useful as a caries detection agent.

Japan was the first country to approve SDF for use as a therapeutic agent in the 1960s. From 1969 onwards, it has been used to arrest carious lesions in children's primary teeth[7,8] and to prevent and arrest root caries in elderly people.[9] SDF has also been shown to reduce dentine hypersensitivity.[10]

SDF was cleared by the Food and Drug Administration (FDA) in the United States in 2014 to treat dentine hypersensitivity entering the US market as Advantage Arrest

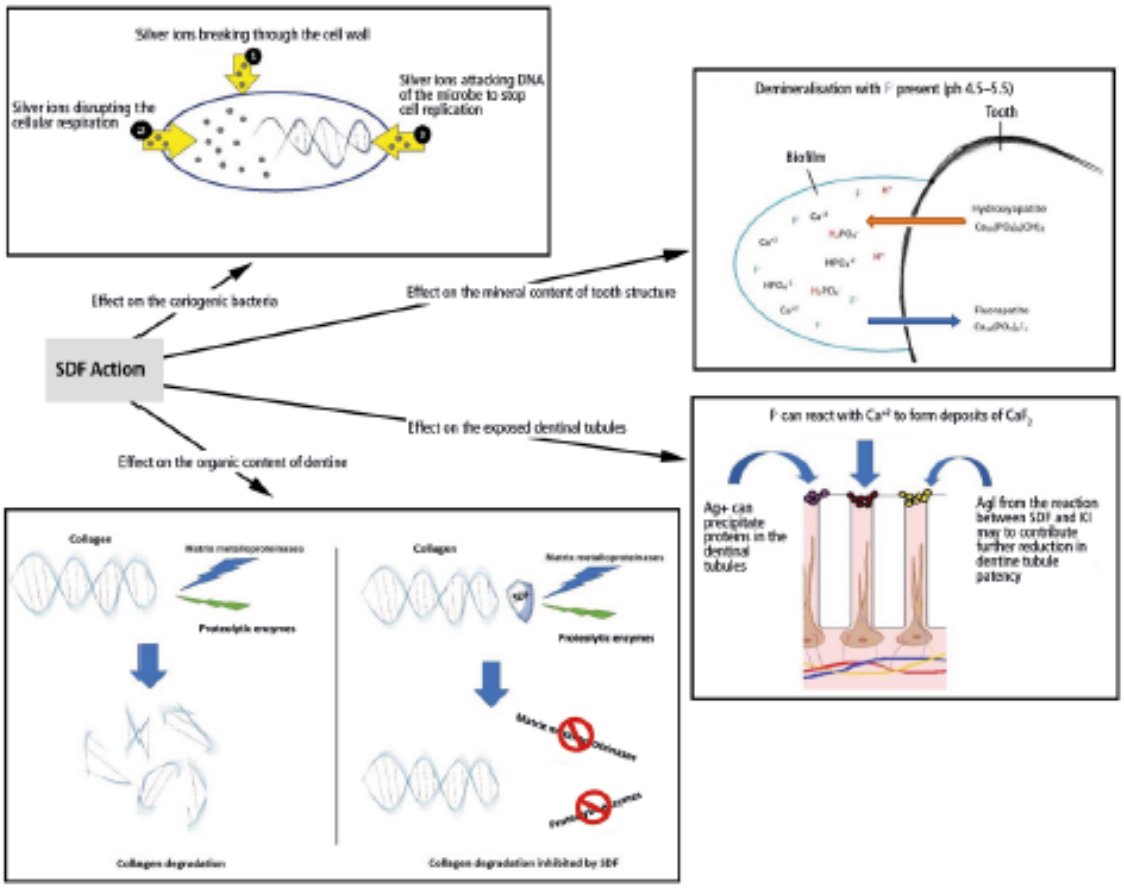

Fig. 1 Diagrammatic representation summarising the main actions of SDF on 1) biofilm bacteria 2) tooth tissue mineral content 3) exposed dentinal tubules and 4) inhibition of collagen (dentine) degradation

Silver Diamine Fluoride 38%, with its use for arresting carious lesions being off-label.[8] It has become recently commercially available in the UK with similar indications, although the only product available in the UK is Riva Star by SDI (SDI, Bayswater, Victoria). Use of Riva Star SDF for caries arrest remains off-label in the UK, in the same way that fluoride varnish preparations (apart from Duraphat) are. This means that although it is not licensed for use for caries arrest, it can be used off-label by licenced professionals when judged by the prescriber to be in the best interests of the patient, on the basis of the available evidence.

As well as Riva Star SDF being available in the UK and Australia, other commercial products are available; Advantage Arrest (US), Saforide (Japan), FAgamin (Argentina), Cariestop (Brazil), and ammonia-free CSDS (Australia).

SDF in the UK; Riva Star (SDF and KI solutions)

The Riva Star product has two coloured capsules; a silver capsule that contains 38% SDF and a green capsule with a saturated solution of potassium iodide (KI) which is claimed to mitigate the black staining of arrested carious lesions. The literature supports 38% SDF as the optimal concentration to arrest carious lesions. KI has been reported to reduce SDF's discolouration by the SDF solution's silver ions reacting with the KI iodide ions forming silver iodide. However, there is conflicting evidence around the success of the KI in avoiding discolouration without it affecting the caries arrest, desensitisation or restoration adhesive properties of the SDF when used alone. The KI solution was initially designed for the margins of restored lesions that had been treated with SDF for desensitising reasons, before glass ionomer being placed (usually for root surface carious lesions) or as a base for permanent molar restorations. There are several reports supporting its use.[11,12] However, more recent ones show the staining still occurs. One *in vitro* study found that SDF's efficacy in stopping secondary caries around the margins of restorations was reduced when KI was added and there was still discolouration when KI was used although this was less than with SDF alone.[13] A clinical trial in an elderly population in Hong Kong[9] found that staining still occurred around the margin of restorations when KI was used. As the Riva Star SDF has a high pH of 13, use of a gingival barrier or rubber dam should be considered to avoid chemical burn of the soft tissue (this differs from Advantage Arrest, pH 10).

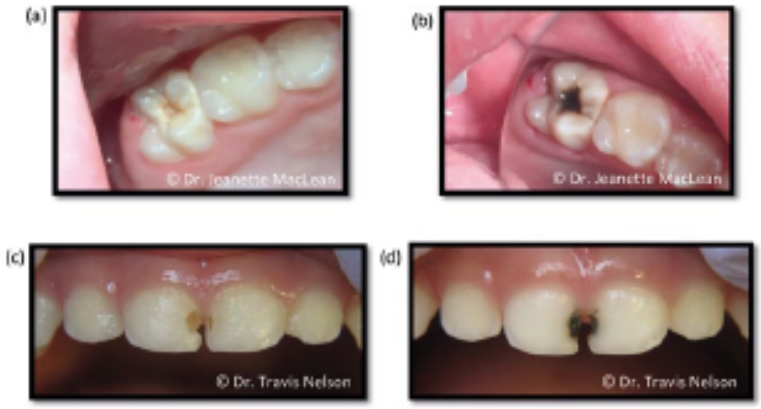

Fig. 2 Clinical photographs before and following application of SDF. (a) Upper right first permanent molar affected on the mesial fossa of the occlusal surface before SDF treatment and (b) several weeks after treatment. (c) Upper primary central incisors with mesial cavitated dentinal carious lesions before SDF treatment and (d) several weeks after treatment

Use of SDF for arresting carious lesions

One of the biggest changes in our understanding of dental caries over the last century is that it is no longer considered an infectious disease but a behaviourally mediated, biofilm-based disease.[3] Until recently carious lesions were managed by the conventional 'drill and fill' philosophy meaning complete carious tissue removal and the replacement of missing tooth tissue with a restoration. This operative or completely surgical approach to dental care, where all carious tissue is removed as a standard part of the procedure to manage the carious tooth, is now challenged to the extent that it is no longer advocated.[14,15] Carious tooth tissue does not always need to be removed to stop the disease progression and in fact, more minimal loss of tooth and less tissue destruction is often a more successful strategy for managing the problem long term.[16,17,18] Good examples of this which have strong evidence to support them are the stepwise carious tissue removal, selective caries removal (previously known as partial caries removal) and the Hall Technique. Restorative approaches must be applied alongside activities aimed at preventing further disease. These activities focus on efforts to modify behaviours that led to the disease in the first place or supported factors leading to the disease (that is, inadequate biofilm removal, remineralisation or high sugar consumption). Methods like this to prevent the establishment of carious lesions can also be used to prevent progression of the disease and, therefore, stop its consequences, especially in primary teeth which exfoliate. So, it is possible to use preventive methods to stop the progression of dental caries rather than removing any of the diseased tissue. In addition to this, it is not always possible, or desirable, to restore the remaining tooth. A non-restorative cavity control (NRCC) option may be possible for managing cavitated lesions.

How SDF is thought to work

SDF's efficacy and clinical effectiveness are well documented in the scientific literature; however its mechanism of action remains contested and only partially understood. A diagrammatic overview of the four main modes of action is shown in Figure 1.

1. Silver ions affect the bacteria by interacting with their proteins and deoxyribonucleic acid (DNA) to inhibit bacterial cell wall synthesis, DNA synthesis and to induce mitochondrial failure.[19] These bactericidal properties cause disruption to the dental plaque biofilm. Demineralised dentinal surfaces treated with SDF have significantly less growth of cariogenic species compared with those not treated with SDF[20,21]
2. Remineralisation of demineralised inorganic tooth mineral is supported by the fluoride ions in SDF and fluorapatite, silver phosphate and calcium fluoride are formed, producing a surface more resistant to acid dissolution[22]
3. Silver precipitates and calcium fluoride can reduce the patency of dentinal tubules
4. SDF has an inhibitory effect on matrix metalloproteinases and cathepsins, the proteolytic enzymes responsible for collagen degradation in dentine when it is undergoing carious destruction.[23,24]

In addition, bacteria killed by silver have a further role in the biofilm's disruption and caries-protection of the whole mouth through the 'zombie effect' whereby living bacteria are killed on contact with silver-affected bacteria.[25]

SDF as part of a non-restorative cavity control option for carious lesions

There are some situations where carious lesions cannot be managed by selective caries removal and restoration. These include, where there is so little tooth tissue structure remaining that no restorative solution is possible and where there is limited or no capacity to cooperate with standard treatments without resorting to general anaesthesia or other forms of sedation. Also, in paediatric and special care dentistry, there is often a need to slow/stop lesion progression and 'buy time' allowing individuals to develop cognitively and/or acclimatise to the dental environment and become more able to cope with restorative treatment solutions. It can also allow time to engage parents/carers in changing behaviour (particularly in relation to diet and oral hygiene), to allow the disease progression to be stopped. This approach avoids the futility of only restoring the result of the problem; similar to 'replacing windows in a burning building'. Finally, sometimes arresting lesions in primary teeth is enough to prevent pain and infection before the teeth exfoliate. SDF may not always be successful and it may not remove the need for an alternative approach which may be restorative, or more invasive, if the lesion does not arrest and continues to progress deeper or increase in size.

SDF as part of a restorative-based option for carious lesions

As well as being a treatment in its own right, SDF can be used as part of a restorative process by following use of SDF by restoration placement. Using SDF alongside atraumatic restorative treatment (ART)[26] is sometimes known as a silver modified ART (SMART) restoration[27,28] or for the Hall Technique as SMART Hall. This can be done either immediately before placing

Table 1 Off-label use of medicines: prescribers' responsibilities (related to use of SDF in Dundee Dental Hospital)

'... you should:'	Justification/ rationale and further information
'be satisfied that an alternative, licensed medicine would not meet the patient's needs before prescribing an unlicensed medicine'	SDF is licenced in the UK as a desensitising agent and cavity cleanser/ conditioner. There is no alternative, licenced medicine.
'be satisfied that such use would better serve the patient's needs than an appropriately licensed alternative before prescribing a medicine off-label'	There is no alternative, licenced SDF product available in the UK
Before ... using a medicine off-label you should:	
'be satisfied that there is a sufficient evidence base and/or experience of using the medicine to show its safety and efficacy'	There are 30 randomised control trials and 11 systematic reviews of variable quality. These have been summarised in a recent Umbrella Review which shows that, despite the variety in populations studied and outcomes measured, there is consistent evidence in favour of SDF as a medicine that, by direct application, can arrest active carious lesions with few documented adverse events
'take responsibility for prescribing the medicine and for overseeing the patient's care, including monitoring and follow-up'	Staff who will use the medication and who oversee patient care have been trained in its use. We monitor and follow-up patients who have been prescribed SDF
'record the medicine prescribed and, where common practice is not being followed, the reasons for prescribing this medicine; you may wish to record that you have discussed the issue with the patient'	The use of SDF, the reasons for prescribing and the discussions that have taken place with children and their parents are recorded in the patient's notes
Best practice for communication includes:	
'you give patients, or those authorising treatment on their behalf, sufficient information about the proposed treatment, including known serious or common adverse reactions, to enable them to make an informed decision'	We have an information leaflet for the parent/ carer's of children whom we are discussing use of SDF with, this is given to them and each section discussed with them, especially the side-effect of discolouration of carious lesions. The leaflet contains pictures of what they might expect for anterior and posterior teeth
'where current practice supports the use of a medicine outside the terms of its licence, it may not be necessary to draw attention to the licence when seeking consent. However, it is good practice to give as much information as patients or carers require or which they may see as relevant'	Current practice in other countries (particularly the US, Australia, Brazil China, Hong Kong and Japan) supports the use of SDF as a cariostatic agent. This information is shared as considered appropriate by the clinician
'you explain the reasons for prescribing a medicine off-label or prescribing an unlicensed medicine where there is little evidence to support its use, or where the use of a medicine is innovative'	There is a body of evidence to support the use of SDF as a cariostatic agent. Its use in this way is not innovative as it has been used as a cariostatic agent for around 50 years in other countries. In addition, the American Dental Association and the American Academy of Paediatric Dentistry recommend and provide guidelines for appropriate use in clinical practice. This information is shared as considered appropriate by the clinician
'Healthcare professionals have a responsibility to help monitor the safety of medicines in clinical use through submission of suspected adverse drug reactions to the MHRA and CHM via the Yellow Card Scheme. Such reporting is equally important for unlicensed medicines or those used off-label as for those that are licensed'	The Yellow Card Scheme is followed and any suspected adverse drug reactions as per protocol are reported

a restoration (using selective carious tissue removal or, in the case of the Hall Technique for primary molars, no carious tissue removal) or after placing SDF then waiting for a few days or weeks until the carious lesions have arrested, sensitivity has resolved or the patient has become acclimatised to the dental environment. Using SDF before restoration placement may reduce the chances of a sealed carious lesion progressing and irreversible pulpitis or dental infection ensuing. However, there are currently no randomised control trials investigating SMART's effectiveness compared to other restorative options.

Studies have shown that SDF has no effect on the bonding of resin composite materials to sound dentine.[6,29] However, the evidence is less consistent regarding glass-ionomer cements (GIC), with some studies suggesting an increase in its bond strength to dentine following SDF application,[30] and others a reduction.[6] Another study has shown that rinsing the mouth with water following SDF application can prevent a significant reduction in bond strength between GIC and sound dentine, therefore rinsing is encouraged when using SDF and GIC to restore a carious lesion directly.[31]

SDF can also play a role in managing dentine hypersensitivity and in managing symptomatic molar incisor hypomineralisation (MIH) affected teeth. Silver ions' ability to occlude dentinal tubules through protein precipitation is well documented.[32] Additionally, SDF placement will stimulate production of calcium fluoride and silver iodide, both of which are able to occlude dentine tubules and reduce their patency.[32,33] Despite SDF's licensing for managing dentine hypersensitivity, there are few trials and no systematic reviews of this topic.

What is the evidence for its use?

A recent umbrella review (a systematic review that, rather than review primary studies, puts together the evidence from systematic reviews) included 11 systematic reviews where SDF was used for carious lesion management in children and adults.[5] The umbrella review found that for prevention of carious lesions in adults and in children, there was insufficient evidence to draw conclusions on the effectiveness of SDF. However, all of the systematic reviews consistently supported the effectiveness of SDF for arresting coronal carious lesions in primary teeth and arresting and preventing root carious lesions in older adults.

Use of a medicine 'off-label'

'Arrested (coronal) (root) caries' is an accepted standard diagnosis listed as code K02.3 in the World Health Organisation's International Statistical Classification of Diseases and Related Health Problems (ICD10)[34] and is the main outcome for the randomised control clinical trials that have been conducted in children and elderly adults.[5] In the UK, Riva Star SDF is licensed for tooth sensitivity and cavity cleansing. Although the main use for SDF seems to be as a cariostatic agent, it does this through its actions of cleansing the cavity of the biofilm (by its bactericidal action) and blocking dentinal tubules to avoid sensitivity.

It is accepted that there are clinical situations where it is in the patient's best interests, on the basis of the best available evidence, to use a licensed medicine 'off-label' that is, using the medicine outside of the terms of the licence.

Table 2 Detailed indications, contra-indications, advantages and disadvantages of NRCC for primary teeth by tooth and person level factors

Uses of SDF		
	Level	**Description**
Indications	Tooth	Asymptomatic cavitated dentine carious lesions in primary teeth
		Lesions that are, or can be made, cleansable
		Non-restorable dentinal lesions
		Several carious lesions that may not all be treated in one visit
		Root surface carious lesions (primary and permanent teeth)
		Non-carious cervical lesions giving sensitivity
		Molar incisor hypomineralisation to reduce sensitivity
	Person	Pre-cooperative children, children and adults whose behaviour/ medical conditions limit invasive restorative treatment and where there is a need to 'buy time' to avoid or delay treatment with sedation or general anaesthesia
		Patients with high caries risk with medical or psychological conditions that limit other treatment approaches eg patient with dental phobia, medical conditions or disabilities
		Patients who already have a high standard of brushing or are likely to be responsive to measures to change behaviour to carry out frequent, high quality toothbrushing or other methods to clean carious lesions
Contra-indications	Tooth	Clinical signs or symptoms of irreversible pulpitis, or dental abscess/fistula
		Radiographic signs of pulpal involvement, or peri-radicular pathology
		Infection or pain from pulp or food packing (unless shape of tooth can be changed to become cleansable)
		Ongoing active lesions that are not arresting (only detectable over time)
	Person	Not able or willing to brush and unlikely to. Patients (or parents) unable or unwilling to take responsibility
		Potassium iodide is contra-indicated in pregnant or breastfeeding women, patients undergoing thyroid gland therapy or on thyroid medication or patients with known allergy to potassium or iodine.
		Patients with ulceration, mucositis, stomatitis.
		Patients with allergy to silver, fluoride or ammonia
Advantages	Tooth	Can help to maintain space in the primary/mixed dentition if avoids the extraction of a tooth/root
	Person	May avoid restorations or dental extractions in patients who would find this difficult to cope with (medically or psychologically)
		Useful for improving cooperation in anxious or pre-cooperative individuals by allowing a minimally invasive treatment then building on successful treatment and coping strategies
Disadvantages	Tooth	Not always successful. Relies to some extent on cleansability and cleansing by the patient/ carer or biofilm profile and these may not be possible to predict
		Difficult to monitor success
		Might not work rapidly enough or with enough success to avoid the pulp becoming irreversibly damaged or infected
	Person	Aesthetics
		Feeling of delaying/avoiding a traditional restorative solution

The UK government services and information website 'Off-label or unlicensed use of medicines: prescribers' responsibilities'[10] gives details of what practitioners should consider in these circumstances (see Table 1 for further details) and although Riva Star SDF is licensed for use in the UK as a desensitising agent, it can be prescribed and used 'off-label' as a cariostatic agent if:

1. There is a body of evidence supporting its efficacy
2. There is no alternative, licensed medicine
3. It is used for this purpose in many other countries; in Canada SDF is approved for the treatment of caries.

In the USA, Advantage Arrest was awarded FDA Breakthrough Therapy Designation for caries arrest in 2016. This prompted clinical trials to demonstrate its efficacy in arresting carious lesions in children aged one year and over. The outcome of these trials will determine whether the FDA will grant SDF a licence for use as a caries arrest agent. The ADA and AAPD both support off-label use of SDF in the US and there is no liability associated with its use when supported by the provider's best clinical judgement and the existing body of evidence on effectiveness and safety.

Indications for SDF

SDF is used as an agent to promote the arrest and remineralisation of active carious lesions. It is effective for active dentinal lesions, teeth with exposed root surfaces causing dentinal hypersensitivity and may also be useful for permanent molar teeth with MIH as blocking the dentinal tubules may reduce sensitivity. It can also be used as a caries detection tool as it stains only carious tooth tissue but it must be remembered that this staining is permanent. Table 2 shows the indications, contra-indications, advantages and disadvantages of SDF and Box 1 shows procedural instructions for its use.

Assessing SDF treatment success

For carious lesions, the success of SDF is assessed by the arrest or progression of the lesion concerned. Traditionally lesion colour was used to determine whether a lesion was arrested. However, this is more accurately assessed by how the lesion feels when a ball-ended probe is dragged across it, rather than by its appearance. For enamel, this relates to its roughness and smoothness (to do with the enamel prisms) and for dentine it is the lesion's hardness and softness (Table 3).

Photography can also be helpful in assessing whether carious lesions have progressed and are more accurate than relying on memory or written descriptions.

For MIH or dentine hypersensitivity, SDF's success is assessed by reduction in sensitivity, usually by an air blast test with the 3 in 1 syringe.

Safety and side effects

Thirty-eight percent SDF contains a high concentration of fluoride ions; 44,800 ppm. However, one drop only contains 2.24 mg of fluoride, compared with a typical dose of 5% fluoride varnish which contains 11.3 mg fluoride. With biannual application dental fluorosis should not be a risk in children.

In addition to the black staining of arrested carious lesions, SDF stains almost everything

Table 3 Tactile and visual characteristics of enamel and dentinal lesion activity (active/ inactive) based on ICDAS-II classifications[38,39]

	Enamel		Dentine	
	Active lesion	Inactive/arrested lesion	Active lesion	Inactive/arrested lesion
Tactile features (by gently running a ball ended probe over the surface)	Rough	Smooth	Soft	Hard
Visual appearance	Dull, matt area although likely to be covered in biofilm	Shiny	Often lighter in appearance but this is not definitive. Likely to be covered in biofilm	Often darker in appearance but this is not definitive. Likely to be free of biofilm

Box 1 Instruction for SDF use

Before use

1. Always handle with care, wear gloves and change them frequently during use to avoid accidental staining of hands or clinic surfaces.
2. Ensure dentist, nurse and patient have personal protective equipment on
3. Obtain informed consent from the patient and, where necessary from their parent/carer.
4. Take photographs at baseline and follow-up appointments to help record and assess the status of carious lesion if these are being treated. If this is not possible, there should be a written record of the status of the lesion.

Clinical application

1. Remove gross debris from cavitation to ensure SDF reaches the carious tooth tissue or area of the tooth it is being applied to.
2. Apply petroleum jelly to the lips to reduce the chance of temporary staining if inadvertent contact with SDF.
3. Isolate the area with cotton roll and apply gingival barrier if the lesion is close to the gingiva (the Riva Star kit has a barrier or use petroleum jelly). Alternatively, rubber dam can be used. However, take care not to coat parts of the carious lesion or tooth tissue it is being applied to.
4. Dry the carious lesion or tooth tissue with a gentle flow of compressed air or a cotton wool roll.
5. Pierce foil on silver capsule with a micro-brush.
6. Apply the SDF with a micro-brush directly onto the lesion or area of tooth being treated.*
7. Allow the SDF to absorb into the tooth via capillary action for at least 1 minute. Try to keep isolated for up to 3 minutes.
8. Blot excess solution to reduce the chance of it contacting the patient's tongue.**
9. 5% NaF varnish may be applied to the area if a carious lesion or MIH affected tooth is being treated as this may help to promote remineralisation.
10. Consider placing a dab of toothpaste on the patient's tongue if they notice a metallic taste

*If using KI, apply immediately after SDF application; pierce the foil on green capsule with a clean micro-brush and apply one to three times until no more white precipitate forms.

** If carrying out a silver modified ART restoration, encourage the patient to rinse after SDF application but before placing the glass ionomer (see text – this does not apply to resin composites)

Follow-up

- Follow-up at 2–4 weeks after the first application to check the activity of the carious lesion. Arrested carious lesions look darker and are hard to the touch i.e. when a ball ended probe is run across the surface. If the carious lesion is still active, a reapplication of SDF could be indicated (see section on assessing treatment success).
- Cavitated lesions can be restored after treatment with SDF. If they are not restored, bi-annual SDF reapplications show a better arrest rate versus one-time application.

it comes into contact with. It should therefore be handled with care. Gloves should be worn when handling it or using it and they should be changed frequently. It should be stored upright in the original box. When it is being used, patients should wear protective eyewear and their clothing should be protected. Petroleum jelly is applied to the peri-oral area to reduce the chance of accidentally staining the lips or face. If staining occurs on the skin, wash off immediately with water or wipe away with a slurry of salt and water. If a stain is left it will behave like a temporary tattoo, like henna, that resolves with the natural turnover and exfoliation of the epithelial cells. Extra attention needs to be paid as Riva Star SDF is a clear liquid, difficult to see and it does not stain immediately but might take (30–60) minutes for the discoloration to become visible. If it is spilled accidentally on clothes or clinical surfaces it could leave a black stain that is difficult to remove. Therefore, if spillage occurs, the surface, should be cleaned immediately with water, bleach, potassium iodide or bleach-containing cleaning products.

A temporary metallic taste might be noticed by patients; however, this goes away rapidly and can be counteracted by a dab of toothpaste on the patient's tongue.

In a study of parental attitudes to staining of primary teeth, parental tolerance was higher for lesion staining for posterior teeth (67.5%) than in anterior teeth (29.7%), unless their child had significant behavioural barriers to dental treatment. In the extreme instance of having to decide between SDF application or their child having a general anaesthetic, parents' acceptance rates of SDF staining increased to 68.5% on posterior teeth and 60.3% on anterior teeth. Parents' acceptance of the treatment also varied according to their socioeconomic status.[86]

Adverse events

No serious adverse events, such as allergic reactions, toxicity or pulpal irritations have been reported in any of the randomised control trials. Gingival reactions and chemical burns to skin were rare.[5] From a pharmacokinetics perspective, SDF use is safe even when applied to several carious lesions at the same visit. There is no quantitative data available for serum toxicity in children following SDF application; however, a recent study measuring adults' serum silver and fluoride ion concentrations after application of SDF to three teeth per participant found that neither silver nor fluoride ions achieved serum concentrations approaching acute toxic levels.[87]

Conclusions

SDF is licensed in the UK for management of dentine hypersensitivity and would also seem to be useful for managing MIH molars that are sensitive. There is a body of evidence to support

its use off-label as a cariostatic agent either on open carious lesions or under restorations in primary and permanent teeth. Clinicians should ensure they explain to patients and parents/carers that it has the side-effect of discolouring carious lesions and prescribe in line with clinical indications as outlined in this paper.

Authors contributions

NI, NS and MR conceived, designed this project and drafted the manuscript. NI, NS, MR, JM, KB, SG, RM and CS Contributed to writing, reviewing and have approved the final manuscript.

Conflict of interest

The Child Dental and Oral Health department were gifted eight boxes of Riva Star from SDI to use at Dundee Dental Hospital and School in 2018. The company have had no say in its use in the department, and have not had any role in conceiving, designing, writing, commenting on or reviewing this paper.

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Publication 4 "It's really no more difficult than putting on fluoride varnish": a qualitative exploration of dental professionals' views of silver diamine fluoride for the management of carious lesions in children

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"It's really no more difficult than putting on fluoride varnish": a qualitative exploration of dental professionals' views of silver diamine fluoride for the management of carious lesions in children

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Abstract

Background: Despite evidence that Silver Diamine Fluoride (SDF) can be effective in managing carious lesions in primary teeth, the use of SDF in the UK remains limited. This study explored dental professionals' views and experiences of using SDF for managing carious lesions in children. In addition, it explored what they perceived to be the advantages, disadvantages, barriers and enablers to the use of SDF in practice.

Methods: Fifteen semi-structured face-to-face or over-the-phone interviews were conducted with 14 dental professionals from NHS Tayside and NHS Grampian in Scotland. Interviews were transcribed verbatim, coded and analysed using a thematic approach.

Results: Thirteen of 14 dental professionals interviewed were familiar with, or had some existing knowledge of, SDF. Four had used it to treat patients. The majority of participants thought that the main advantage of SDF was that it required minimal patient cooperation. SDF was also perceived as a simple, pain-free and non-invasive treatment approach that could help acclimatise children to the dental environment. However, SDF-induced black staining of arrested carious lesions was most commonly reported as the main disadvantage and greatest barrier to using it in practice. Participants believed that this discolouration would concern some parents who may fear that the black appearance may instigate bullying at school and that others may judge parents as neglecting their child's oral health. Participants thought that education of clinicians about SDF use and information sheets for parents would enhance the uptake of SDF in dental practice. Participants believed that younger children might not be as bothered by the discolouration as older ones and they anticipated greater acceptance of SDF for posterior primary teeth by both parents and children.

(Continued on next page)

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Conclusion: Dental professionals were aware that SDF can be used for arresting carious lesions. They pointed out that the staining effect of carious lesions is a major disadvantage and had preconceived ideas that this could be a barrier for many parents. Participants considered the application process to be simple and non-invasive and requires a minimum level of child cooperation. Participants appreciated the potential of SDF in paediatric dentistry and suggested actions that could help overcome the barriers they highlighted.

Keywords: Silver diamine fluoride, Caries, Non-restorative caries treatment, Dental professionals, Barriers, Enablers

Background

Dental caries is the most prevalent chronic disease in the world [1]. In recent years, as a result of a better understanding of the pathology of the disease, there has been a shift from traditional 'drill-and-fill' techniques towards more minimal-intervention, evidence-supported treatment options, such as Atraumatic Restorative Treatment, the Hall Technique (HT) and fluoride agents [2]. The effectiveness of fluoride-based materials for preventing and arresting carious lesions is well-established [3, 4].

Silver nitrate was first reported as effective in arresting carious lesions in the 1840s [5] and G.V Black described protocols for its use in the early 1900s [6]. This paved the way for another silver product; silver diamine fluoride (SDF) to be developed. Silver diamine fluoride was first explored as a treatment option for managing carious lesions in Japan in 1969 [7]. It is a clear, odourless liquid [8] containing silver and fluoride, which act synergistically to arrest carious lesions through a variety of mechanisms [9]. Silver ions interact with the bacterial cell wall and enzymes to inhibit bacterial growth. They can also integrate into hydroxyapatite and have an antibacterial effect on silver-integrated hydroxyapatite. Furthermore, silver ions can inhibit cathepsins and dentine collagen degradation. On the other hand, fluoride can promote remineralisation by forming fluorohydroxyapatite with reduced solubility. It can also inhibit matrix metalloproteinases activities and therefore dentine collagen degradation [10].

Silver diamine fluoride was cleared by the Food and Drug Administration in the United States in 2014 for managing dentine hypersensitivity [11]. Since then, there has been growing interest in its "off-label" use for managing carious lesions, supported by reports of its effectiveness, with a recent umbrella finding it effective in arresting carious lesions in children [12].

There are two additional benefits of SDF as a treatment to arrest dental caries. Firstly, it is a non-aerosol generating procedure so can be applied in a way that does not increase the risk of transmission of acute respiratory infection (such as COVID-19 [13]) in the dental surgery. Secondly, it can be applied in settings other than the dental surgery because it does not require specialist dental equipment other than a mirror, tweezers and cotton wool.

It is well reported that the translation of evidence into practice is slow, unpredictable and can be met with resistance [14, 15]. The implementation of research findings requires more than simply producing and disseminating recommendations and clinical guidelines [16]. Despite its availability in the UK since April 2016 [17], use of SDF at the beginning of 2020 was still limited to dental schools and a small number of practices in the UK. Furthermore, there is scant research exploring Dental Professionals' (DPs) views about using SDF to manage carious lesions in children [18–21]. Identifying the barriers and facilitators to its use in practice, from the perspective of DPs, may facilitate the development of strategies and interventions to improve its uptake.

This paper presents the findings from a qualitative study undertaken with DPs to explore their views, including their perceived barriers and enablers, to the use of SDF for the management of dental carious lesions in the primary dentition.

Methods

Study design

This study comprised semi-structured telephone and face-to-face audio recorded interviews with a purposive sample of DPs. Interviews took place between December 2018 and June 2019. The consolidated criteria for reporting qualitative research (COREQ) [22] were used as a guide to ensure quality.

Participants and recruitment

To ensure sample diversity, a purposive strategy was adopted [23]. Dental Professionals who could apply topical fluoride or who were involved in its use, were considered eligible for inclusion. These included practicing dentists, dental therapists, dental hygienists and dental nurses, of any age. These clinicians were treated as a single group and no comparisons of views across professionals were made. Participants did not need to have previous experience of SDF application to take part.

Participants were recruited in two Scottish Health Boards (HBs) (NHS Grampian and NHS Tayside),

through a Teaching Dental Hospital, general dental practices, Vocational Trainee Dental Practices, Public Dental Services and the Scottish Dental Practice Based Research Network's database (SDPBRN) of Rapid Evaluation Practices.

Dental professionals were sent an invitation pack containing an information sheet, a reply slip and a freepost envelope. Participants were invited to return the reply slip in the freepost envelope or contact the researcher directly by telephone or email.

Consent and ethical review

Prior to the interview, participants were given the opportunity to ask any questions and confirm they were happy to take part, and consent was explained and obtained. For face-to-face interviews, the consent process was carried out in person, while for over-the-phone interviews consent was discussed and then agreement to participate (if given) was audio recorded before the audio-recorded telephone.

This study was approved by University of Dundee Schools of Nursing, Health Sciences and Dentistry Research Ethics Committee (application number: 2018 012_Seifo). The study was approved by the Research and Development Managements at NHS Tayside and NHS Grampian (IRAS ID: 252305).

Data collection

Face-to-face to interviews took place at the workplace with the presence of the researcher and the participant only. Interviews were semi-structured using open-ended questions and probing. A topic guide was developed to explore the following: DPs existing knowledge and experience of SDF; perceived advantages and disadvantages to its use; barriers and enablers to SDF for the management of carious lesions in the primary dentition; and DPs views of children's and parents/carers' acceptability of SDF (Additional file 1: Interview topic guide).

The topic guide was piloted with two DPs and amended accordingly to ensure face validity. Data from pilot interviews were not included in the analysis. Interviews continued until data saturation was achieved, i.e. when no new themes or categories were emerging from the data. Interviews were carried out by one researcher NS who has experience of performing interviews as well as training in qualitative data management and analysis.

Data handling and analysis

All audio recordings were securely transferred to a professional transcription service and transcribed verbatim. All identifiable data were anonymised. Transcripts were accuracy checked prior to analysis. Data were managed using NVivo 12 software QSR (International Pty Ltd., Melbourne, Australia). Thematic analysis was undertaken using the framework approach as a broad guide to organise and classify data according to key issues, concepts and emerging themes [24]. These interviews were exploratory, with the aim of identifying the advantages, disadvantages, barriers and enablers for using SDF in practice. It was therefore important that the method of analysis allowed for the identification of key issues using the topic guide as a broad framework as well as recognising other emergent themes.

To minimise bias and ensure consistency, a sample of transcripts were double coded independently and in duplicate by NS and HC (an experienced qualitative researcher).

A coding framework was developed following the initial review of three transcripts. This was then assessed by an independent researcher (HC), not involved in conducting the interviews. Development of the codebook was an iterative process with adaptations made through discussion as appropriate. The codebook is available on request.

Patient involvement

Patients were not involved in this study.

Results

Fifteen interviews were conducted (13 face-to-face and two by telephone) with 14 participants. One participant was interviewed twice, once prior to, and again after, applying SDF for the first time. No participants contacted refused to participate. Six participants worked within primary care and eight within secondary care. Of the 14 participants, 12 were dentists (nine general dental practitioners, one consultant, one core trainee and one vocational trainee), one dental therapist and one dental nurse. Nine of the14 participants were female. The age of participants ranged from 25 to 61 years with a clinical experience ranging from one to 33 years. Five participants had used SDF before. Most interviews lasted, on average 25 min in duration (ranging from 10 to 35 min), A few of the interviews were shorter when participants did not have much to discuss i.e. had not had considerable knowledge, or experience with SDF.

DPs' perceptions about using SDF in practice

The vast majority of those interviewed were aware of SDF and were able to articulate that it can be used for arresting carious lesions in children. A small number also identified that it can be used to treat dentine hypersensitivity or knew that it can be used as a topical fluoride to prevent caries. The black staining of arrested carious lesions was raised by most participants.

> *"Um, so I know that it's a method for arresting carious lesions, uh, and quite like with stainless steel*

crowns, it has a similar challenge, sometimes, to present to the parents that it's not going to be very aesthetic because it's going to stain them black"
DP 12 (Dentist).

Four participants reported that they had experience applying SDF before participating in the interviews although one was on extracted teeth only. One DP, a dental therapist, had not applied SDF at the time of their initial interview, however, had a patient booked in for SDF application. A second interview was conducted with this participant to gather feedback and explore their initial thoughts and experience. This made the total number of interviewed DPs with experience of SDF five. It was noted that that these five participants were all employees of Dundee Dental Hospital and School.

DPs' perceived advantages of SDF

When participants were asked about the advantages of using SDF over other dental treatments, the majority highlighted that minimum cooperation was required; this could potentially be beneficial for children or patients with special needs or dental phobia. One dentist commented that this could result in reduced referrals to secondary care. It was however also highlighted that a degree of cooperation would still be required, given that SDF is prone to staining with anything it comes into contact.

"I think it'll be good for patients who we've got very little cooperation ..... So I think the children who have got developmental issues or erm, a low tolerance for dental treatment will be very good because there'll be limited time where they're in the chair"
DP 3 (Dental nurse).

The majority of DPs suggested that they believe SDF to be a simple, easy and non-invasive approach for managing carious lesions in children because there is no requirement for local anaesthetic, use of rotary instruments or even excavating carious tissues. One dentist who had used SDF several times commented:

"I think it's, it's very easy, it's very easy to do, it's um, it doesn't require us to do anything that a child will, will find particularly traumatic at all... Erm, it's really no more difficult than putting on fluoride varnish"
DP 2 (Dentist).

Contrary to this, one dentist commented that not requiring an injection was not necessarily a unique advantage of SDF, highlighting other approaches used in children's dentistry, such as HT.

Participants also suggested that due to being pain free and minimally invasive, SDF may help to acclimatise children to having dental treatment, helping them to be more aware of the dental environment and more accepting of more complex dental procedures in future visits. It may also help build a cooperative non dental-phobic patient through their adult life.

DPs perceived disadvantages and barriers of SDF

The majority of participants were concerned with the aesthetic outcomes of SDF treatment and suggested that the permanent discolouration of arrested carious lesions could potentially be a barrier to parents' acceptability of its use. SDF can also stain the oral mucosa, skin and the clinic surface. Therefore, DPs highlighted that meticulous attention is required while applying it to avoid any inadvertent spillage or contact. Riva star™ (SDI Limited, Bayswater, Australia), which is the commercial SDF product available in the UK, is a clear solution. One dental therapist who reported having used this particular product reported that they found it inconvenient to use, because it was difficult to notice any accidental spillage before staining occurs.

"Um, I would say the biggest disadvantage with something like silver diamine fluoride would be that get-getting patients to accept it, the fact that it might... they've maybe got lesions that are just pale brown or you know, not very highly coloured, when you paint this on it'll actually turn them black so it'll look quite unsightly"
DP 8 (Dentist).

Participants believed that the aesthetics associated with SDF application would be the largest barrier from the parent's and child's perspective. There was an assumption, even from those who had not used SDF before, that parents may not agree to its use. Reasons given for this included, a fear of their child being bullied or a fear of judgment from others, who may think that they are not looking after their child's teeth.

"Um, I think there are some children where, um, if their teeth go dark chocolate brown they might get picked on at nursery or at school and, um, that certainly – I have met children where that has been an issue"
DP 4 (Dentist).

Given the additional possibility of inadvertently staining the skin or the gingiva, one dentist suggested that parents may hesitate about choosing SDF unless they fully

trusted the DP applying it. One participant mentioned having encountered patients reluctant to receive any fluoride treatment. They believed that SDF would not be an option for these patients:

> *"There are some parents who believe fluoride is a poison and that is their belief and, um, despite the fact that you and I might think otherwise..."*
> **DP 4 (Dentist)**.

Another disadvantage highlighted was the unpleasant taste or sensation attributed to SDF. In addition, participants with experience of applying SDF highlighted that it was not easy to access interdental lesions in posterior teeth unless the lesion was fully cavitated. In addition, food packing in that area might obstruct SDF from reaching the whole carious lesion. It was noted that the size of the micro-brush supplied with the SDF kit was not sufficiently small to access fully all interdental lesions in posterior teeth.

A number of participants suggested that the lack of training and information available about using SDF was a barrier to its use in general dental practice. However, this was less of an issue for DPs working within Dundee Dental School who reported that they had received training on its use.

> *"I mean, obviously, I work in a teaching hospital so I get exposed to new techniques and things, but people in practice, unless they go on courses to learn how to use it, if they weren't trained with it, they might be very reluctant to use it not knowing anything about it"*
> **DP 1 (Dentist)**.

It was suggested that introducing a new fluoride agent into practice may be challenging due to another type of fluoride based preventive material, Fluoride Varnish (FV), having been used in practice for a significant period. In addition, since SDF is licenced for treating dentine hypersensitivity, using it to arrest carious lesions would be deemed "off-label". Indeed, for this reason, some of those interviewed suggested they would be hesitant to use it, with one DP querying whether there could be legal implications using this "off-label".

> *"The off licence to me is more of an issue if you're trying to get it used in general practice because personally, I would feel less comfortable. Doesn't mean I wouldn't use it, it just means that I would be a bit more cautious in how I'd approach the children"*
> **DP 2 (Dentist)**.

Dental Professionals working within NHS primary care highlighted an additional barrier with SDF not currently listed in the Scottish Statement of Dental Remunerations (SDR). As a result, practitioners in Scottish NHS primary care practices would not be able to claim financially for applying this agent.

DPs' perceived enablers of SDF use

As well as capturing potential barriers to using SDF in practice, factors to enable its use were also explored. It was suggested that the lack of training opportunities available could be addressed with the development of new training courses or Continuous Professional Development events which may in turn encourage use in practice. In addition, educating DPs about the implications of using agents "off-label" would mitigate such concerns.

> *"Um, so I think for me it was a barrier initially. Um, but then the more I read about it I realised that being used off licence is okay... Um, so I'm very happy to do it now"*
> **DP 2 (Dentist)**.

It was suggested that in order to facilitate the introduction of SDF to parents, an information sheet, explaining the associated advantages, disadvantages and expected outcomes, with photographs demonstrating arrested carious lesions, could help.

> *"It would be nice to have something official in place that they could read as well, that's probably a good consideration"*
> **DP 12 (Dentist)**.

A few participants suggested that improving the evidence base around the use of SDF for arresting carious lesions in children and restricting or minimising the staining effect could increase implementation. It was also suggested that the introduction of SDF into the SDR would allow NHS primary care practitioners to claim for it, hence removing the financial barrier. Figure 1 summarises the perceived barriers and enablers to using SDF in practice.

DPs' perceived uses of SDF

The DPs Interviewed for this study believed that SDF would be a useful option for children unable to cooperate or tolerate other treatment approaches. One dentist went on to say that SDF should be limited to uncooperative children but could also be used for adults with dental anxiety or special needs. The majority of participants agreed that SDF would be particularly beneficial in avoiding or delaying the use of General Anaesthesia (GA) and intimated that parents would rather their child had black teeth, whether in the posterior or anterior

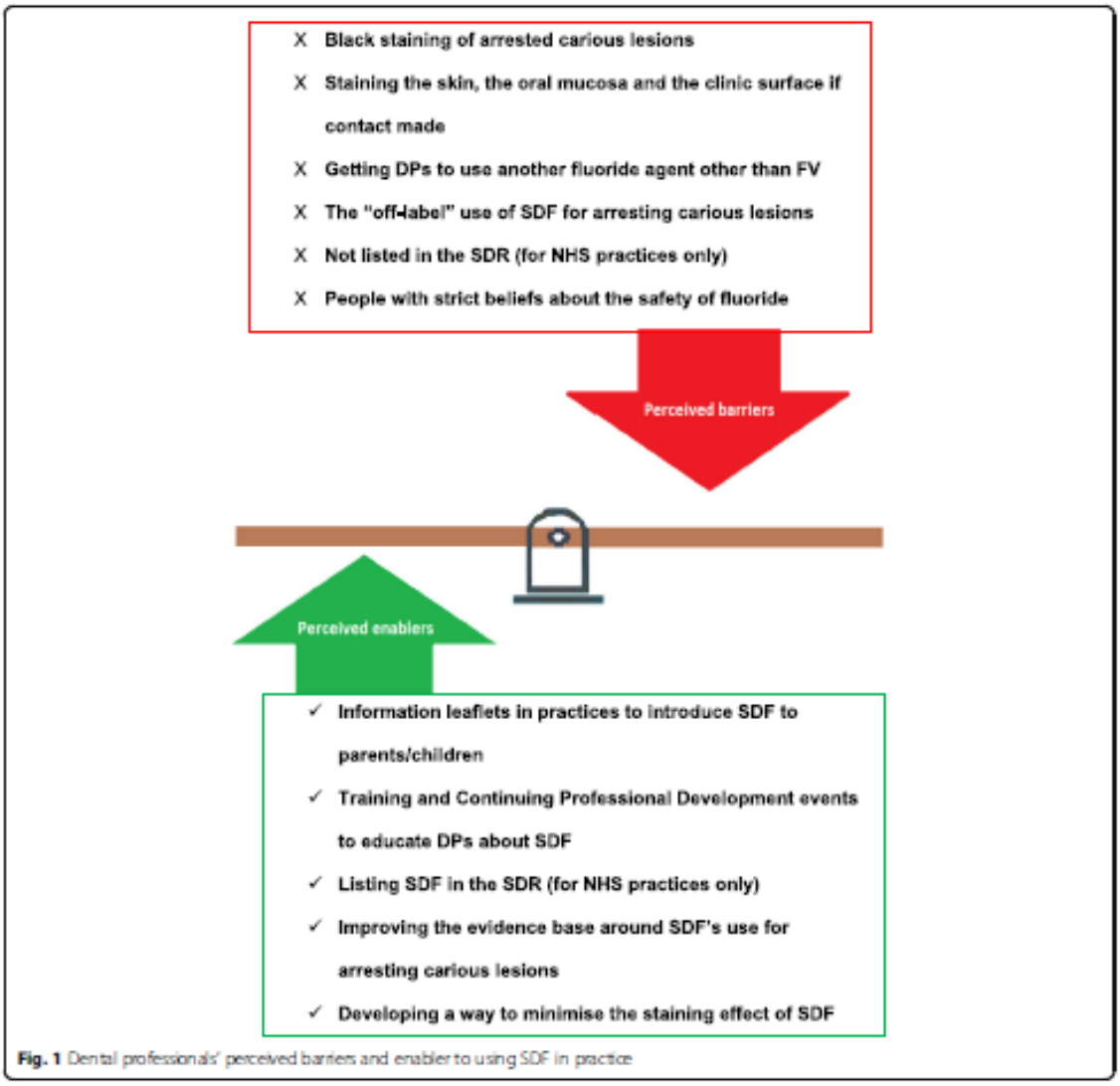

Fig. 1 Dental professionals' perceived barriers and enabler to using SDF in practice

sextants, if this avoided their child having a GA. A dental therapist who had experience of applying SDF on a three-years old boy's anterior and posterior carious lesions commented:

> *"Uh, I didn't really need to convince her (the child's mother). She was happy to do it if it's a possibility of avoiding a general anaesthetic"*
> **DP 5 (Dental therapist).**

One dentist identified another potential advantage of SDF was that applying it does not require any complex or advanced equipment, making it particularly useful in developing countries or areas with limited resources. Some DPs also suggested that SDF would be especially valuable where a child has multiple carious lesions, where treating all lesions would normally require several dental appointments. Applying SDF on all carious lesions during one appointment could result in both time and cost savings.

> *"you've often got the situation where a child has got lots of teeth that need treatment, um, so you could quite easily apply SDF on everything, even at one visit. And that would be a quick, cost-effective way of getting it done"*
> **DP 1 (Dentist).**

DPs' views of SDF compared to HT

Some of those interviewed raised points about the similarities between SDF and the HT. The HT has become increasingly popular in children's dentistry and has been proven to be effective for managing carious lesions in primary teeth [25]. This was a theme which emerged from the initial few interviews and as a result the interview topic guide was adapted to specifically explore DPs perceptions of the relative advantages and disadvantages of both SDF and the HT. Some DPs interviewed during this study suggested that SDF would be more comfortable for the child due to the simple application process involved, whereas the HT can be uncomfortable when seating the crowns.

> *"I mean certainly we do use the Hall crown a, a lot and you know, the Hall Technique and that's, that's very effective. But even then there are certain things you've got to do with it that maybe are slightly uncomfortable you know, putting the separators, actually seating the crowns, um, and they can be quite difficult, quite challenging if the crown, if it's difficult to match the crown size to the tooth"*
> **DP 8 (Dentist)**.

Participants stated that placing the HT requires more cooperation, as fitting the HT crowns has more steps and takes more time than applying SDF.

> *"Um, however, I guess the downside of the Hall crown is it does need a little bit more cooperation to do I think than SDF, um, because you need to seal it and remove cement and things like that"*
> **DP 9 (Dentist)**.

It was still felt however, that when it comes to SDF, parents may be more sceptical about its effectiveness due to the lesion being left open, and food might keep packing in the area. The area would require careful tooth cleaning to remove the debris. It was suggested that parents may feel more confident about the use of the HT due to the lesion being covered and because it may not require the same level of follow-up care.

> *"The only thing about the Hall crown is at least the parent thinks it's covered so they don't have to pay so much attention to cleaning they would think in their head, you know, they think oh, it's covered up whereas they'd be more worried about, "Oh, you're just putting a paint on and darkening it, you haven't actually fixed the hole". So in their head they think why haven't you fixed the hole?"*
> **DP 11 (Dentist)**.

DPs' views regarding parents'/children's acceptability of SDF

Participants had mixed views about how parents may feel about SDF. Some participants believed parents would be reluctant to have SDF used on their children, due to the discolouration of the teeth, while others thought they would not mind the appearance of SDF treated carious lesions.

> *"The downside is it does look black so you will get some parents that'll say, "No, my kid's not having that done", I'm sure"*
> **DP 1 (Dentist)**.

These beliefs were explored further in the interviews, as were the factors that DPs believed may influence parents' decision-making. Some participants suggested that fathers may be less concerned about the appearance of their child's teeth after treatment especially if it was simple and pain-free, whereas mothers may be more concerned about the aesthetics. One participant however, disagreed with this viewpoint:

> *"Um, no, I, I don't think a mother versus father's opinion would be different"*
> **DP 7 (Dentist)**.

Child gender was identified by participants as a potential influence with some participants suggesting that girls are generally more self-conscious than boys. Other participants however, thought that gender would not impact upon the child's decision-making around SDF. The age of the child at the time of treatment was also identified as potentially influencing parents' decision-making with some participants suggesting that parents of younger children (six or younger) would be less concerned about discoloration, believing that younger children may not be as self-conscious. It was also perceived that there would be less opposition to SDF being applied to posterior rather than anterior teeth.

When exploring children's acceptability of SDF, DPs suggested that children generally preferred what they consider to be the least invasive treatment and, therefore, may choose SDF, despite the discolouration. One dentist interviewed suggested that while younger children may be less bothered by the staining, they may also be influenced by their parent's views.

> *"Yeah, younger kids wouldn't be as self-conscious. They haven't got the capacity to determine that, unless of course mummy says it's horrible-looking then they're probably not going to be very happy with it either"*
> **DP 12 (Dentist)**.

Participants believed that older children can be more self-conscious and more accepting of SDF for their posterior teeth, but less so for anterior teeth and may be influenced by their social environment, and therefore may be influenced by other factors, such as the school they attend and the views of their peers.

> *"I think it, I think it depends on what environment they're in, so depending on what school they're at and the type of school that they're at, 'cause children can be cruel"*
> **DP 3 (Dental nurse).**

Discussion

This qualitative study found that DPs' knowledge and experience of SDF varied significantly, from being unaware of it prior to the interview, to having used it in practice. They saw the main advantages centring on its non-invasive nature and the low levels of patient co-operation required to apply it. The most significant barrier identified was discolouration of the treated tooth and DPs' concern about parent and child acceptance of this. It was agreed however, that parents and children may be more accepting of SDF and the discolouration associated with it, when treating non-visible lesions or when used in place of more invasive treatments or GA. These findings echo previous survey data on DPs' perceptions and attitudes toward SDF [18–21], which identified a lack of knowledge about SDF, discolouration as a barrier for parents and highlighted the need for education regarding usage. This seems to be the first qualitative study to explore DPs' perceptions of SDF use. Qualitative research enables the identification of issues a priori and allows deeper insight into attitudes, not possible through quantitative research [26].

Of the 14 interviewed DPs, 13 had some previous knowledge of SDF. Dental professionals working within a dental school setting, or who had recently graduated, were more informed than those working in general practice for longer. Of the few DPs who had applied SDF, all worked at Dundee Dental Hospital. By working within an educational institution, they may have been more likely to be exposed to novel and innovative treatment approaches. Silver diamine fluoride was licenced in the UK in April 2016 [17] and the interviews were conducted in (December 2018 – March 2019).

The most commonly reported advantage of SDF by the DPs, was that applying it required less compliance on the part of the child, particularly in comparison to other procedures used to manage carious lesions. As a result, SDF was seen as potentially beneficial in acclimatising children to the dental environment, supporting them towards accepting more invasive dental procedures in the future. This is particularly important because traumatic dental experiences, particularly in childhood, have been linked strongly to the development of dental anxiety and dental phobia through adulthood [27].

The most commonly reported disadvantage of SDF, in line with previous studies [28], was the permanent black staining of the arrested carious lesions caused by the formation of silver phosphate [29]. One other perceived disadvantage related to the commercial Riva Star™, SDF product, is that it is a clear solution. This makes accidental spillages difficult to see. Not all SDF products, have this issue, for example Advantage Arrest™ (Elevate Oral Care LLC, West Palm Beach, Florida, USA), marketed in the USA is blue in colour making it easier to spot any inadvertent spillage.

In addition to these clinical level barriers, clinicians believe that parents and children may find the colour change a barrier to accepting the treatment. This has been reported in the literature as a significant disadvantage [20, 28, 30]. The rationale given by DPs was that they thought parents might worry that their child would be bullied at school or nursery because of their physical appearance. Globally, 15.3% of students who have been bullied report being made fun of because of how their face or body looks [31]. They also suggested that parents may be concerned that others would think they have neglected their child's oral health. DPs considered another potential parental concern would be the potential of accidental contact staining of the gingiva and skin.

Some DPs reported encountering patients who believed that fluoride is harmful despite the assurances of health organisations. There is a small proportion of the population likely to be reluctant to receive any treatment that contains fluoride and their perspective has to be respected. However, raising awareness of the benefits of fluorides in children's dental health, while addressing people's concerns, may alleviate some of these concerns [32].

Fluoride varnish is routinely used and national guidance recommends it is applied twice a year for prevention of carious lesions in children aged two and over [33]. Introducing a new fluoride agent and asking clinicians to change well established practices and behaviours may be challenging. Although the indications for SDF and FV overlap but there are some distinct differences. Fluoride varnish is effective at preventing carious lesions [4] whereas SDF's effectiveness seems to lie more in arresting them [12] and it is more effective than FV in this respect [34]. Recommendations that FV is applied following SDF [35], might promote both materials' complementary actions [9, 36]. Furthermore, despite evidence of effectiveness and national guidance promoting its use [33], 12 of the 14 NHS Boards in Scotland have not met the UK Government's HEAT target for FV applications in 2015 [37]. Factors influencing this low uptake remain

unclear, however possible explanations are that some DPs are not convinced about the effectiveness of such preventive approaches, or some parents are reluctant to have fluoride therapy for their child.

Some of those interviewed reported that they would be hesitant to use SDF as this would need to be "off-label". In the UK prescribers can use a product in this way provided they are satisfied that an alternative, licensed medicine would not meet the patient's requirements and it would serve their needs better, based on the available evidence supporting its efficacy and safety [38]. Although this is common practice in medicine, raising awareness around this for dental prescribers may be required.

To facilitate SDF use, minimising discolouration would seem beneficial. Riva Star™ provide encapsulated potassium iodide KI for application immediately after SDF. However, a recent systematic review [39] reported conflicting evidence and uncertainty for the effectiveness of SDF + KI in mitigating the long-term staining effect of SDF. Even though some studies reported a positive association between SDF + KI and minimal discolouration, other studies refuted these findings while others reported an increased blackening over time.

National clinical guidelines are considered a reliable information source to improve the quality of clinical decision making and assure clinicians about the appropriateness of the treatments they provide [40]. Therefore, incorporation of SDF into clinical guidelines could encourage uptake. This would ideally go hand in hand with remuneration for SDF being incorporated into the SDR as some DPs believe that not being able to claim a fee for its use, is a further practical barrier to using SDF in NHS practices.

Alongside guidance, training events or workshops to familiarise DPs with SDF when it is appropriate to use it as an "off-license" product were suggested by DPs as helpful in overcoming some of their perceived barriers. Having an SDF information sheet in practice was also suggested to help with the introduction of SDF to parents. This would support parents to judge whether the advantages of using SDF outweigh the disadvantages in their individual situation and facilitate decision-making regarding their child's dental treatment.

Dental professionals believed that SDF may be particularly useful for very young children and those who cannot tolerate other treatments. It could act as a transitional treatment until the child is more able to cooperate. However, it may also be a final treatment if the parents/child do not mind the discolouration. SDF's ease of use is relevant for older children or adults who cannot tolerate standard treatments for medical or psychological reasons i.e. frail elders or adults with physical disabilities or dental phobias. However, further research to support the effectiveness of SDF in arresting coronal carious lesions in the permanent dentition is needed [41]. This unique benefit of SDF could potentially reduce referrals for GA for some patients. Those living in more in areas with less access to dental care may also benefit as it does require complex equipment for its application. Finally, SDF may also be beneficial where a patient has several lesions that cannot be managed in one. The time lag between appointments in these situations may increase the risk of existing lesions progressing and becoming symptomatic. Applying SDF to all lesions would arrest them and control the disease while awaiting the completion of the treatment.

Interestingly, DPs compared SDF application with placement of crowns using the HT since they share some common clinical indications. Participants believed that SDF would be more convenient for the child than the HT which requires placing elastic separators and scheduling a second visit to fit the crown. Furthermore, seating the crown can result in disruption of the occlusion and the child may experience discomfort after the crown is placed, albeit this resolves within 24 h. Participants also perceived that lower levels of child cooperation would be required when applying SDF but expressed awareness that unexpected movements could result in oral mucosa, skin or clinic surface staining, so a degree of co-operation was still required. Another stated benefit was that SDF could be applied to several carious lesions even on two occluding teeth at the same appointment whereas the HT has some restrictions, for example, it cannot be used on two occluding teeth until the occlusion becomes re-established with bilateral contacts.

For this study, purposive sampling was undertaken to ensure sample diversity. Participants were recruited through primary and secondary care from two NHS Health Boards (HBs) in Scotland. These findings may however be generalisable across the whole UK, considering the similarity in the training DPs receive across UK NHS HBs. It should be noted however, that the primary aim of qualitative research is to gain a greater understanding of opinions and trends and not necessarily identify issues that are generalisable. Furthermore, the remuneration system is not necessarily the same across the four countries of the UK, which in turn may influence the uptake of a specific treatment unless it is listed in all four SDRs in the UK i.e. if SDF is introduced first in the Scottish SDR, it is only logical that a higher uptake of SDF would be in Scotland than the rest of the UK. In order to minimise researcher bias, a proportion of interview transcripts were double coded independently by two authors (one clinical and one non-clinical experienced qualitative researcher).

However, there are a few caveats that should be kept in mind when interpreting the results of this study. Nine

out of the 14 DPs who were interviewed had not had experience with SDF before and therefore, their views may change after applying it. In addition, because SDF was only introduced into the UK recently, DPs who had used it before, had limited experience and will not have had the opportunity to follow up patients over extended periods of time. Seeing patients over longer timeframes, allows clinicians to understand long-term outcomes associated with treatment and gain deeper understanding of the impacts on the child and family. It could be the case that with greater experience and follow up with patients, the DPs' perceptions of the treatment may change. In addition, the interviews were conducted during the working day with busy healthcare professionals and it may be that they condensed their responses or were very focussed in their conversation due to time pressures. However, all participants completed the interview as planned and were asked if there was anything else they wished to add at the end of the interview. As a result, it is unlikely any important contributions were missed.

This study focused on DPs attitudes and acceptability of SDF. These are vital because if DPs are reluctant to use or even learn about SDF, they will not adopt it and parents will not have the opportunity to find out about SDF in the first place. Research exploring the views of parents and children and their acceptability of SDF will complete a fuller picture around the use of SDF in practice.

Conclusions

Dental professionals were aware that SDF can arrest carious lesions but saw staining of the carious lesion as its major disadvantage and had preconceived ideas that parents would find the appearance a barrier. They considered the application process to be simple, non-invasive and less challenging of child cooperation than other dental procedures, but that a minimum level of compliance would still be required. Dental professionals believed that SDF is a valuable addition to their paediatric dentistry treatment procedures and were prepared to suggest actions that could be taken to reduce each of the barriers they noted.

Supplementary information

Supplementary information accompanies this paper at https://doi.org/10.1186/s12903-020-01243-y.

Additional file 1. Interview topic guide.

Abbreviations

SDF: Silver diamine fluoride; DP: Dental professional; SDPBRN: Scottish Dental Practice Based Research Network; FV: Fluoride varnish; HT: Hall technique; HB: Health Boards

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Authors' contributions

NS, HC, JR and NI designed the project and drafted the protocol. NS conducted the interviews and collected the data. NS, HC and NI analysed the data. NS, HC, JR and NI read, revised and approved the final manuscript.

Authors' information

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Availability of data and materials

The datasets used and analysed during the current study and a description of the coding tree are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

This study was approved by University of Dundee Schools of Nursing, Health Sciences and Dentistry Research Ethics Committee (application number: 2018012_Seifo). The study was approved by the Research and Development Managements at NHS Tayside and NHS Grampian (IRAS ID: 252305). A written consent for face-to-face, and audio recorded consent for phone interviews, were obtained from participants prior to participation.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Publisher's Note

Publication 5 The efficacy of silver diamine fluoride in arresting caries in children

The efficacy of silver diamine fluoride in arresting caries in children

Abstracted from

Chibinski AC, Wambier LM, Feltrin J, Loguercio AD, Wambier DS, Reis A.

Silver diamine fluoride has efficacy in controlling progression in primary teeth: A systematic Review and meta-analysis. *Caries Res* 2017; **51:** 527-541.

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Question: Is silver diamine fluoride (SDF) more effective than other active treatments/placebo in arresting caries in children?

Data sources PubMed, Scopus, Web of Science, the Latin American and Caribbean Health Sciences Literature database (LILACS), the Brazilian Library in Dentistry (BBO), Cochrane Library and grey literature.

Study selection Two reviewers selected randomised clinical trials (RCTs) that compared the efficacy of SDF application with other active treatments or placebo in arresting carious lesions.

Data extraction and synthesis Three authors extracted data using customised extraction forms, and risk of bias was assessed by two independent reviewers. Meta-analyses were performed on studies classified at 'low' or 'unclear' risk of bias, where similar outcomes were recorded in primary teeth, and that compared SDF to active treatments.

Results Eleven studies were included; five studies were at 'low', two at 'unclear' and four studies at 'high' risk of bias. Eight were conducted with primary teeth, two with permanent first molars and one conducted on both. Six studies used 38% SDF, two 30% SDF, one 12% SDF, one compared 38% SDF to 12% SDF and one used Nano Silver Fluoride (NSF).

Meta-analysis was performed on four studies conducted in primary teeth. The arrest of carious lesions at 12 months was 66% higher (95% CI 41–91%; $p < 0.00001$) with SDF than with other active materials, but it was 154% higher (95% CI 67–85%; $p < 0.00001$) when compared to placebos. Overall, carious lesion arrest was 89% higher (95% CI 49–138%; $p < 0.00001$) than using active materials/placebo. No heterogeneity was detected.

Conclusions SDF is more effective than active treatments or placebo for carious lesion arrest in primary teeth. The body of evidence was of high quality for primary teeth. However, there was not enough high quality evidence to draw conclusions about carious lesion arrest in first permanent molars.

Commentary

Despite significant advances in dental care over the last few decades as well as the inception of the World Health Organization (WHO) Global Oral chronic diseases affecting people from different countries (35% of people have untreated caries in permanent teeth and 9% of children experience untreated caries in primary teeth) and across all age groups,[1] and a 2013 Health Programme to increase the awareness of oral health world-wide,[2] dental caries is still one of the most prevalent diseases.

Conventional dental treatment to manage carious lesions can be time consuming and expensive, and in some cases, (eg children, those with disabilities, elderly or individuals with dental fear) these approaches may not be feasible, due to affordability or inability to cope with invasive treatment. Moreover, current research suggests that carious lesions do not always need to be managed using a traditional 'drill and fill' approach and can be both managed and arrested using alternative and more cost-efficient methods.[3] Silver diamine fluoride (SDF) is a water-like liquid that is applied to teeth with active carious lesions using a microbrush. Its use aims to arrest the progress of the disease by interfering with the carious process, the dental tissues and the microflora involved. SDF has been the subject of a resurge in interest in silver-based products (another one is silver nitrate) One side-effect of SDF is that it causes blackening of carious lesions. This might be seen by the dental profession as a significant disadvantage but there is little research investigating this. However, at least for the children, one report has noted that parents have seen this colouration as a positive indication that the treatment was effective.[4]

The aim of this systematic review was to explore the evidence for the effectiveness of SDF in arresting carious lesions in primary teeth and first permanent molars, after it was cleared by the Food and Drug Administration (FDA) for dental use in the US in 2014[4] and becoming commercially available in the UK as Riva Star by SDI recently.

An extensive database search and reference lists hand-searching was conducted with no restrictions on publication date or language. Quality assessments of included trials were evaluated by two independent reviewers using the Cochrane tool. Sequence generation and allocation concealment were considered the two key domains out of the six domains in the Cochrane risk of bias tool. The quality of the evidence, assessed using Grading of Recommendations, Assessment, Development and Evaluations (GRADE), was high for the single outcome that could be analysed (caries arrest at 12 months). Heterogeneity was assessed using

the Cochrane Q test and I2 statistics. All analyses were conducted using RevMan (version 3, the Cochrane Collaboration, USA).

The authors have stated that two reviewers classified the full texts that met the inclusion criteria and three extracted the data. However, it is not clear if these were performed independently. Included trials used different concentrations of SDF, apart from one trial that used Nano Silver Fluoride, which was developed to replace SDF as it does not stain carious lesions.

It was not possible to conduct meta-analysis on data from permanent teeth because they reported different outcomes and contacts with the authors were not successful in gaining enough information to overcome this problem. However, a meta-analysis (with four studies) was performed on studies conducted in primary teeth where similar outcomes were recorded, and which were evaluated as 'low' or 'unclear' risk of bias in the key domains. The meta-analysis broke the studies into two sub-groups; one with two studies where SDF was compared with other active materials (such as fluoride varnish and Atraumatic Restorative Treatment) and the other sub-group of two studies, where placebos were used. Both sub-groups showed consistent results favouring SDF as effective for arresting carious lesion in primary teeth.

There are five other published systematic reviews investigating the effectiveness of SDF for caries management in children.[5-9] However, this review has overcome many of the limitations seen in the other reviews, such as failure to compare similar outcomes, evaluate risk of bias of the included studies or include languages other than English during the search. Another measure of the quality of this review is that the authors preregistered their protocol in the PROSPERO database (CRD42016035741) and adhered to their published plan.

This well conducted systematic review has raised a critical question about the effectiveness of SDF in arresting caries in children and endeavoured to answer it in the most appropriate way. Although the other systematic reviews all were positive about the clinical effectiveness of SDF, they had significant potential for biases and many were conducted so long ago that very few trials were included. On the other hand, this systematic review with high quality methodology and including eleven studies presents the most robust evidence so far supporting the use of SDF. Unfortunately, there is not enough evidence make a judgment on the effectiveness of SDF in first permanent molars in children and more clinical trials will be required to provide this. However, in primary teeth, it is evident that SDF is statistically and clinically more effective than other active treatments/placebo in arresting carious lesions after 12 months.

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APPENDICES

Appendix 1 an umbrella review of silver diamine fluoride for managing carious lesions: effectiveness and adverse events (protocol)

available at:

https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=70063

Nassar Seifo, Heather Cassie, John Radford and Nicola Innes

Background

Despite significant advances in dental care over the last few decades as well as the improvement in people's dental knowledge, dental caries is still one of the most prevalent chronic diseases affecting people from different countries and across all age groups (Marcenes et al., 2013).

Conventional dental treatment for caries can be time consuming and expensive, and in some cases, for example with children, those with disabilities, populations with low access and institutionalized elderly, these approaches may not even be feasible, due to lack of ability to cope with treatment, access traditional dental care or pay for it. In addition, recent understanding of the disease of dental caries has shown that it does not always need to be managed by a traditional “drill and fill” approach and the disease can be managed and arrested through other approaches (Ricketts et al., 2013, Schwendicke et al., 2016). As a result, alternative, low cost treatments options have been investigated (Frencken et al., 2012).

Clinical trials with different focuses and approaches have suggested the use of 38% silver diamine fluoride (SDF) for carious lesion management (Llodra et al., 2005, Zhi et al., 2012, Duangthip et al., 2016). Fluoride has proven to be effective in enhancing the remineralization of dental hard tissues (Marinho et al., 2013) while silver ions act upon cariogenic bacteria, and it has been used to arrest caries in Japan since the 1960s (Yamaga and Yokomizo, 1969, Marinho et al., 2013) and since then there has been a growing interest in SDF (Chu and Lo, 2008).

However, one of the disadvantages of using SDF is that the carious lesion will be stained black after its application. In addition, it can stain clinic surfaces and clothes, which does not wash away once it sets. Moreover, SDF also stains the skin causing painless 'temporary tattoo' which cannot washed away easily, but disappears after few days with the natural exfoliation of skin. Additionally, accidental contact of SDF with oral mucosa or gingiva may cause irritation represented in mildly painful white lesion, which heals spontaneously in 48 hours (Horst et al., 2016).

Several reviews with different perspectives and of varying quality have examined the literature around SDF (Rosenblatt et al., 2009, Gao et al., 2016). With the increase in the number these synthesizing and appraising evidence on SDF, a logical next step to provide decision makers in healthcare with the evidence they

require to inform practice, is to conduct a review of these existing systematic reviews. This will allow their findings to be compared and contrasted and to see if the different perspectives they have taken and the breadth of their focus can help give more in-depth information to the wider picture of how we can expect SDF to perform, for example, in various clinical settings, with different populations, in groups with different caries rates or in lesions in primary compared with permanent teeth.

Aim

The aim of this review is to assess systematic reviews and meta-analyses investigating the effectiveness of SDF in arresting and preventing caries in primary and permanent teeth (coronal and root caries).

Methodology

To ensure a high-quality methodology, we have followed the methodology proposed by the Joanna Briggs Institute for conducting an umbrella review (Aromataris et al., 2015).

Search strategy

A systematic search will be performed across five databases: PubMed (MEDLINE), EMBASE, Cochrane Database of Systematic Reviews, Joanna Briggs Institute Database of Systematic Reviews and Implementation Reports and the PROSPERO register between the years 1970 and 2017.

Searches will be built around these key words: "silver diamine fluoride" OR "silver diammine fluoride" OR "diamine silver fluoride" OR "diammine silver fluoride" OR "silver fluoride" AND "caries" AND "systematic" OR "meta-analysis" for databases which do not have a predefined search filter designed to identify review articles.

No restrictions will be placed on the language of reviews during the search.

Criteria for including reviews in this review

Types of reviews

Systematic reviews and meta-analysis comparing the use of SDF with any other intervention or placebo or no treatment, in adults or children for prevention or management of dental caries.

Types of participants

Children and adults with or without carious lesions in primary and/or permanent teeth.

Types of interventions

Topical application of any concentration or duration of application of SDF for prevention or management of dental caries with or without caries excavation compared to any other intervention including placebo or no treatment.

Types of outcomes and outcome measures

- Caries prevention, as measured by change from baseline in the number of decayed missing, filled permanent teeth/surfaces (DMFT/S), and decayed missing filled primary teeth/surfaces (dmft/s) or other similar outcomes and outcome measures that are used.

- Caries arrest indicated by change from baseline from active to arrested caries, measured by visual changes in enamel and dentine or any other outcomes and outcome measures used to evaluate caries arrest.

- We will include a narrative report of other kinds of outcomes and outcome measures that are recorded in the reviews where these cannot be quantitatively synthesised.

Selection of reviews

The publications retrieved from the searches will be combined and de-duplicated in one database Screening of the titles and abstracts titles and abstracts of these reviews will be carried out independently and in duplicate by two authors. Non-systematic reviews and irrelevant systematic reviews will be excluded, reviews that meet the inclusion criteria will be included in this review. All publications assessed as potentially eligible at this stage will be included for the next round of screening.

Full texts of those assessed as potentially eligible from title and abstract screening will be retrieved and two independents investigators will screen the publications independently and in duplicate to assess eligibility. Where there are discrepancies, a third investigator will be consulted, and discussion will take place before making a final decision.

A manual search will be performed on the bibliographies of these reviews to identify relevant papers, which may be included for assessment.

Inclusion and exclusion criteria

Systematic reviews and meta-analysis comparing the use of SDF with any other intervention or placebo or no treatment, in adults or children for prevention or management of dental caries will be included while none-systematic reviews and irrelevant systematic reviews will be excluded.

Dealing with missing data

Authors of the selected reviews will be contacted for unclear methodology, missing or unclear information and missing data.

Data extraction

To minimise risk of bias in the review process, a standardised and piloted data extraction tool will be employed by two independent reviewers to extract data from each included review. Guided by the data extraction tool, information extracted from each included review should include the following:
(1) Citation details
(2) Objectives of the included review

(3) Type of review
(4) Participant details
(5) Setting and context
(6) Number of databases sourced and searched
(7) Date range of database searching
(8) Publication date range of studies included in the review that inform each outcome of interest
(9) Number of studies, types of studies and country of origin of studies included in each review
(10) Instrument used to appraise the primary studies and the rating of their quality
(11) Outcomes reported that are relevant to the review question
(12) Method of synthesis/analysis employed to synthesise the evidence
(13) Comments or notes the review authors may have regarding any included study

Critical appraisal

To assess the quality of the systematic reviews, the AMSTAR tool– 'a measurement tool to assess the methodological quality of systematic reviews' – will be used (Shea et al., 2007). The quality of the systematic reviews will be assessed independently and in duplicate by two reviewers with discussion to reach consensus where there are discrepancies.

Data analysis and synthesis

We will construct a Table of Included Review Characteristics. We will not present primary research study level data (except in the case of there being only one study to inform an outcome).
We will present a summary of the range of interventions used (for example, different strengths and application frequency for SDF), comparisons, outcomes and outcome measures and other issues that are of interest.
We will report on overlap of the primary studies in each review e.g. where studies have been included in multiple reviews.
To present the findings and results, where we find overall effect estimates in the syntheses, through meta-analyses or other techniques, we will present the data in a table with the number of studies and participants that informed each outcome. Where no effect estimates have been calculated, we will state this, to help identify gaps in the evidence. We will also report heterogeneity. The overall direction of findings will be reported. A summary of evidence table linked to this will be constructed showing interventions, included research synthesis and indicating the results of the intervention as being more effective, having no effect or being less effective than the comparator.

Discussion

There are a number of different systematic reviews of the effectiveness and efficacy of SDF, but these include a variety of searches, included studies and populations. By carrying out this umbrella review, we aim to clarify the state of the evidence around SDF in a transparent way, providing context for a variable findings and allowing clarity over the evidence available and what it means for decision making in dental healthcare as well as informing the direction of future research in the area of SDF.

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Appendix 2 Umbrella review search strategy

1- (silver diamine fluoride[Title/Abstract])
2- (silver diammine fluoride[Title/Abstract])
3- (diamine silver fluoride[Title/Abstract])
4- (diammine silver fluoride[Title/Abstract])
5- (silver fluoride[Title/Abstract])
6- (cari*[Title/Abstract])
7- (decay*[Title/Abstract])
8- (cavit*[Title/Abstract])
9- (Meta-Analysis[ptyp])
10-(systematic[sb])
11-#1 OR #2 OR #3 OR #4 OR #5
12-#6 OR #7 OR #8
13-#9 OR #10
14-#11 AND #12 AND #13

Appendix 3 Data extraction tool

<table>
<tr><td colspan="4">Review title:</td></tr>
<tr><td colspan="4">Citation details:</td></tr>
<tr><td colspan="4">Objective of the review:</td></tr>
<tr><td rowspan="6">Methodology</td><td colspan="3">Databases searched and sourced:</td></tr>
<tr><td colspan="3">Date range of database searching:</td></tr>
<tr><td colspan="3">Language restriction:</td></tr>
<tr><td>Outcomes</td><td colspan="2">Primary outcome:</td></tr>
<tr><td></td><td colspan="2">Secondary outcome:</td></tr>
<tr><td colspan="3">Instrument used to appraise studies:</td></tr>
<tr><td></td><td colspan="3">Method of synthesis/analysis to synthesis the evidence:</td></tr>
<tr><td rowspan="6">Results</td><td rowspan="3">Total numbers of papers retrieved from the search:
Additional papers identified:
Papers after duplicates removed:
Titles and abstracts screened:
Full papers retrieved:
Number of papers included:</td><td colspan="2">Inclusion criteria:
Participants:
Intervention:
Comparisons:
Outcomes:</td></tr>
<tr><td colspan="2">Exclusion criteria:</td></tr>
<tr><td colspan="3">Type of included studies:</td></tr>
<tr><td colspan="3">Countries origin of included studies:</td></tr>
<tr><td colspan="3">Publication date range of included studies:</td></tr>
<tr><td>Meta-analysis</td><td colspan="2">Meta-analysis conducted?</td></tr>
<tr><td></td><td colspan="2">Number of studies included in meta-analysis: 2</td></tr>
<tr><td colspan="2" rowspan="2">Review authors comments regarding any included study:</td><td colspan="2">Limitations:</td></tr>
<tr><td colspan="2">Conclusion:</td></tr>
<tr><td colspan="2" rowspan="2">Additional interpreters' comments:</td><td colspan="2">Limitations:</td></tr>
<tr><td colspan="2">Conclusion:</td></tr>
</table>

Appendix 4 ROBIS: Tool to assess risk of bias in systematic reviews

Phase 1: Assessing relevance (Optional)

ROBIS is designed to assess the risk of bias in reviews with questions relating to interventions, aetiology, diagnosis and prognosis. State your overview/guideline question (target question) and the question being addressed in the review being assessed:

Intervention reviews:

Category	Target question (e.g. overview or guideline)	Review being assessed
Patients/Population(s):		
Intervention(s):		
Comparator(s):		
Outcome(s):		

For aetiology reviews:

Category	Target question (e.g. overview or guideline)	Review being assessed
Patients/Population(s):		
Exposure(s) and comparator(s):		
Outcome(s):		

For DTA reviews:

Category	Target question (e.g. overview or guideline)	Review being assessed
Patients):		
Index test(s):		
Reference standard:		
Target condition:		

For prognostic reviews:

Category	Target question (e.g. overview or guideline)	Review being assessed
Patients:		
Outcome to be predicted:		

Intended use of model:		
Intended moment in time:		

Does the question addressed by the review match the target question? YES/NO/UNCLEAR

Phase 2: Identifying concerns with the review process

DOMAIN 1: STUDY ELIGIBILITY CRITERIA
Describe the study eligibility criteria, any restrictions on eligibility and whether there was evidence that objectives and eligibility criteria were pre-specified:
1.1 Did the review adhere to pre-defined objectives and eligibility criteria? Y/PY/PN/N/NI 1.2 Were the eligibility criteria appropriate for the review question? Y/PY/PN/N/NI 1.3 Were eligibility criteria unambiguous? Y/PY/PN/N/NI 1.4 Were all restrictions in eligibility criteria based on study characteristics appropriate (e.g. date, sample size, study quality, outcomes measured)? Y/PY/PN/N/NI 1.5 Were any restrictions in eligibility criteria based on sources of information appropriate (e.g. publication status or format, language, availability of data)? Y/PY/PN/N/NI
Concerns regarding specification of study eligibility criteria LOW/HIGH/UNCLEAR Rationale for concern:

DOMAIN 2: IDENTIFICATION AND SELECTION OF STUDIES
Describe methods of study identification and selection (e.g. number of reviewers involved):
2.1 Did the search include an appropriate range of databases/electronic sources for published and unpublished reports? Y/PY/PN/N/NI 2.2 Were methods additional to database searching used to identify relevant reports? Y/PY/PN/N/NI 2.3 Were the terms and structure of the search strategy likely to retrieve as many eligible studies as possible? Y/PY/PN/N/NI 2.4 Were restrictions based on date, publication format, or language appropriate? Y/PY/PN/N/NI 2.5 Were efforts made to minimise error in selection of studies? Y/PY/PN/N/NI
Concerns regarding methods used to identify and/or select studies LOW/HIGH/UNCLEAR Rationale for concern:

DOMAIN 3: DATA COLLECTION AND STUDY APPRAISAL	
Describe methods of data collection, what data were extracted from studies or collected through other means, how risk of bias was assessed (e.g. number of reviewers involved) and the tool used to assess risk of bias:	
3.1 Were efforts made to minimise error in data collection?	Y/PY/PN/N/NI
3.2 Were sufficient study characteristics available for both review authors and readers to be able to interpret the results?	Y/PY/PN/N/NI
3.3 Were all relevant study results collected for use in the synthesis?	Y/PY/PN/N/NI
3.4 Was risk of bias (or methodological quality) formally assessed using appropriate criteria?	Y/PY/PN/N/NI
3.5 Were efforts made to minimise error in risk of bias assessment?	Y/PY/PN/N/NI
Concerns regarding methods used to collect data and appraise studies	LOW/HIGH/UNCLEAR
Rationale for concern:	

DOMAIN 4: SYNTHESIS AND FINDINGS	
Describe synthesis methods:	
4.1 Did the synthesis include all studies that it should?	Y/PY/PN/N/NI
4.2 Were all pre-defined analyses reported or departures explained?	Y/PY/PN/N/NI
4.3 Was the synthesis appropriate given the nature and similarity in the research questions, study designs and outcomes across included studies?	Y/PY/PN/N/NI
4.4 Was between-study variation (heterogeneity) minimal or addressed in the synthesis?	Y/PY/PN/N/NI
4.5 Were the findings robust, e.g. as demonstrated through funnel plot or sensitivity analyses?	Y/PY/PN/N/NI
4.6 Were biases in primary studies minimal or addressed in the synthesis?	Y/PY/PN/N/NI
Concerns regarding the synthesis and findings Rationale for concern:	LOW/HIGH/UNCLEAR

Y=YES, PY=PROBABLY YES, PN=PROBABLY NO, N=NO, NI=NO INFORMATION

Phase 3: Judging risk of bias

Summarize the concerns identified during the Phase 2 assessment:

Domain	Concern	Rationale for concern
1. Concerns regarding specification of study eligibility criteria		
2. Concerns regarding methods used to identify and/or select studies		
3. Concerns regarding used to collect data and appraise studies		
4. Concerns regarding the synthesis and findings		

RISK OF BIAS IN THE REVIEW	
Describe whether conclusions were supported by the evidence:	
A. Did the interpretation of findings address all of the concerns identified in Domains 1 to 4?	Y/PY/PN/N/NI
B. Was the relevance of identified studies to the review's research question appropriately considered?	Y/PY/PN/N/NI
C. Did the reviewers avoid emphasizing results on the basis of their statistical significance?	Y/PY/PN/N/NI
Risk of bias in the review	RISK: LOW/HIGH/UNCLEAR

Y=YES, PY=PROBABLY YES, PN=PROBABLY NO, N=NO, NI=NO INFORMATION

Appendix 5 Dental Professionals' views of silver diamine fluoride for the management of carious lesions in children: a qualitative study (Protocol)

Nassar Seifo, Heather Cassie, John Radford and Nicola Innes

1. Background

Dental caries (tooth decay) is still one of the most prevalent chronic diseases affecting people from different countries (35% of permanent teeth and 9% of primary teeth have untreated dental carious lesions) and across all age groups (Marcenes et al., 2013). This is despite significant advances in dental care over the last few decades, as well as the inception of the World Health Organization Global Oral Health Programme to increase the awareness of oral health worldwide (Petersen, 2008).

Conventional dental treatment for managing carious lesions is expensive (Listl et al., 2015). In addition, it may not be suitable in certain groups such as children with dental anxiety or disabilities. Current research suggests that dental caries can be managed without using a traditional "drill and fill" approach and instead the process can be arrested using less invasive and more cost-effective methods (Schwendicke, 2017).

Silver diamine fluoride (SDF) has been found to be effective in carious lesion management by arresting the lesion's progression and thereby reducing associated pain and infection (Llodra et al., 2005, Zhi et al., 2012, Duangthip et al., 2015).

One side effect of SDF is that the carious lesion becomes stained black after application. However, it has been suggested that parents may view this discoloration as a positive indication that the treatment is effective (Horst et al., 2016). A survey-based study carried out in the US in 2017, found that staining on posterior teeth was more acceptable than staining on anterior teeth and although staining on anterior teeth was undesirable, most parents preferred this option to invasive behavioural management techniques such as sedation or general anaesthesia (Crystal et al., 2017).

Little attention has been paid to the preferences of DCPs for different treatment options for managing dental caries in the primary dentition in children. This is despite the delay in implementing new techniques into dental practice, even when efficacy has been proven. In particular, little is currently known about the preferences of DCPs i.e. dentists, dental therapists, dental hygienists or dental nurses, in relation to the use of SDF for the management of carious lesions in children.

2. Study rationale

There is evidence that SDF can be used to arrest dental caries, however its application causes black discolouration of the carious lesions. SDF has recently become available for use in the UK. This study will therefore explore DCPs views regarding acceptability of its use for the management of dental carious lesions in primary teeth.

Exploring the acceptability, as well as the potential barriers and enablers to the use of SDF as a treatment approach for DCPs, will contribute to the design of implementation strategies for the use of SDF in clinical practice.

3. Research question/aim(s)

Aim
To explore, with a focus on SDF, DCPs' views regarding treatment options to manage dental carious lesions in the primary dentition.

Objectives
The specific study objectives are to explore:

- the key barriers and enablers to the use of SDF for the management of the carious primary dentition;
- whether previous clinical experience impacts upon preferred treatment approaches; and
- DCPs views regarding children and parents/carers acceptability of SDF

4. Methods

Study design
Semi-structured audio recorded telephone or face-to-face interviews with DCPs.

Participants
A purposive sample of DCPs from across Scotland. An initial recruitment target of 20 DCPs will be sought but will be guided by data saturation. Francis et al. recommend that a minimum of 10 interviews be conducted for initial data analysis, followed by three additional interviews until no new themes emerge. (Francis et al., 2010)

Recruitment
Participants will be recruited through Dundee Dental School and Hospital (DCPs who have a focus on children), the Scottish Dental Practice Based Research Network's (SDPBRN) database of Rapid Evaluation Practices (REPs) through the SDPBRN's Director, Vocational Dental Practices in the East and North East Regions' Training schemes through the Associate Postgraduate Dental Dean-VT Lead and the regional VT advisors and NHS Grampian and NHS Tayside Public Dental Services; formerly known as Salaried Dental Services through the Clinical Dental Directors for each region.
The PI will provide the appropriate person (who has a routine access to potential participants) with an invitation pack containing a participant information sheet and invitation to participate, a reply slip and a freepost envelope that will be sent to potential participants. They will have the option to return the reply slip in the freepost envelope provided or contact the PI directly by phone or email. Follow up phone calls will be made by the PI to interested participants in order to screen for eligibility, discuss the study in further detail and arrange a convenient date and time for interview.

Prior to the interview, potential participants will be given the opportunity to ask any questions and confirm they are happy to take part, and consent will be explained and obtained. For face-face interviews, the consent will be taken in person following TASC SOP07, while for over-the-phone interviews the consent

will be explained and then audio recorded before the audio-recorded telephone interview.

Withdrawal procedure
Participants have the right to withdraw at any stage in the study without giving any reason. If a participant withdraws we will ask if they will allow us to continue to use the data already collected and if they do not wish this, their data will be deleted. All data collected prior to their withdrawal will be kept confidential and will be anonymised in the same way as for other participants.

Data collection
Semi-structured telephone or face-to-face interviews using open-ended questions and probing will be used to collect data. Interviews will be conducted by the PI either over the telephone or face-to-face in a suitable venue. An interview topic guide has been developed to explore the acceptability of and barriers and enablers to the use of SDF, as well as the impact of previous experience and their perceptions of children's and parent/carers' preferences.
The topic guide has been piloted with dental team members to ensure the questions are clear and easy to understand. Revisions were made as appropriate. All interviews will be audio recorded with participant consent. It is anticipated that interviews will last no longer than one hour and will take place during working hours, in line with participants' availability. Data collection will be carried out until data saturation is achieved i.e. when no new themes, categories or explanations are emerging from the data in line with the recommendations made by Francis at al. (Francis et al., 2010)

Data analysis
Analysis will be conducted by the PI using the framework approach to qualitative data management. This is a matrix based method, using a thematic framework to organise and classify data according to key issues, concepts and emerging themes (Spencer and Ritchie, 2002). Data management will be facilitated using NVivo software, which is produced by QSR International (*https://www.qsrinternational.com/*). All interviews will be recorded and transcribed in full; a sample of interviews will be transcribed by the PI and the rest will be transcribed via transcription service (NJC Secretarial). However, all identifiable data will be anonymised before they are transferred to third party, service for transcription. Audio recordings and transcripts will be uploaded into NVivo to facilitate data management.
The five stages of data analysis using the framework approach will then be conducted;

1- **Familiarisation:** This involves the researcher re-listening to all interview recordings and reading through the transcripts and any notes taken at the time of the interviews. This will provide the researcher with an opportunity to articulate and note down some initial thoughts and themes.
2- **Identifying a thematic framework:** During this process the researcher can draw upon a priori issues and, therefore, the initial framework is often largely descriptive and rooted within these a priori issues.
3- **Indexing:** This is where the data is applied to framework headings and involves identifying sections of the text that are associated with these. This process will inform the development of sub-themes. It may be that sections of the text are aligned to two or more themes and when new sub-themes

emerge, the researcher will revisit previous transcripts to establish if they are common themes. This process will ensure saturation of themes.

4- **Charting:** This involves applying the data from the individual transcripts to the index, this information is then extracted from its original context and rearranged according to the key themes emerging from the data as a whole. This will allow comparisons to be made across participants e.g. parents, children, different healthcare professional roles.
5- **Mapping and interpretation:** The final stage will draw together the key characteristics of the data and interpret it as a whole. This will involve comparing and contrasting experiences and perceptions and explore similarities and differences across the data to provide explanations.

The Consolidated Criteria for Reporting Qualitative Research (COREQ) will be employed to guide reporting of the data (Tong et al., 2007).

5. Ethical and Regulatory Considerations

Research Governance
For the duration of the study, all paperwork with study data will be stored securely in a locked cabinet within University of Dundee, only accessible by the main investigators. Digital, anonymised data in the form of interview recordings and transcriptions will be stored in an encrypted and password protected University of Dundee secured database. Data will be available and ready for an audit if required. All data will be archived and stored securely for five years after completion of the project in line with University of Dundee policy.

Consent
Prior to interview, the PI will discuss the study with the participants and they will have the chance to ask any questions, and consent will be explained and obtained. For face-face interviews, the consent will be taken in person following TASC SOP07, while for over-the-phone interviews the consent will be explained and then audio recorded; the PI will read the statement (audio-recorded) and the participant will reply (audio-recorded), then the PI will complete the paper consent form with recorded time, day, participant's answers and will sign the form.

The consent will include critical and important actions that may be carried out during the interview (voice recording, details on interview nature, purpose of the interview, etc.).

Assessment and management of risk
If a participant feels distressed or uncomfortable during an interview, the interview will be terminated immediately, and voice recording will be stopped. A supportive conversation would take place and the participant would be asked if they wish to continue the interview or terminate it.
Research Ethics Committee (REC) review and reports
The study will be conducted in accordance with the principles of Good Clinical Practice. In addition to sponsorship approval, ethical favourable opinion will be obtained from the University of Dundee. Annual reporting will be conducted in compliance with Tayside Medical Science centre requirements.

Peer review

This project has been designed and the protocol iteratively reviewed by three experienced reviewers who are the PI's PhD supervisory team. The project is the partial fulfilment of a PhD in Dentistry and will be examined through Viva Voce examination. The PI's work will be examined, and peer reviewed by an internal examiner from University of Dundee as well as an external examiner from another University Institution.

Data protection and patient confidentiality

All records will be identified in a manner designed to maintain participants confidentiality. All records will be kept in a secure storage area with limited access to study staff only.

Data management will be conducted in compliance with TASC SOPs on Data Management, including TASC SOP53 Data Management Systems in Clinical Research.

[The data management system (DMS) will be NVivo as approved by Sponsor.]

The DMS will be based on the protocol for the study and individual requirements of the investigators. The study master file will collect only information that is required to meet the aims of the study and to ensure the eligibility and safety of the participant. The study database will be compliant with TASC SOP53 Data Management Systems in Clinical Research.

The database is managed in line with all applicable principles of medical confidentiality and data laws. The Data Controller will be the University of Dundee and the Data Custodian will be CI. Database lock will be conducted in compliance with TASC SOP32 Locking Clinical Study Databases.

The PI and study staff involved with this study will not disclose or use for any purpose other than the performance of the study, any data, records, or any other unpublished, confidential information disclosed to those individuals for the purpose of the study. Prior written agreement from the Sponsor or its designee will be obtained for the disclosure of any said confidential information to other parties.

Participants must know the purpose of data collection and be informed how these data will be manipulated and used and the length of data being hold securely. Participants' permission is mandatory for the audio recording that will be anonymised using a study ID number (all personal data will be deleted prior to transcription) and only the study researchers will access the anonymised transcriptions of audio recording.

The PI and study staff involved with this study will comply with the requirements of the Data Protection laws with regards to the collection, storage, processing and disclosure of personal information. The PI and study staff will also adhere, if appropriate, to the current version of the NHS Scotland Code of Practice on Protecting Patient Confidentiality. Access to collated participant data will be restricted to the CI and appropriate study staff.

Computers used to collate data will have limited access measures via user names and passwords.

Published results will not contain any personal data that could allow identification of individuals participants

Insurance and Indemnity

The University of Dundee and Tayside Health board are Co-Sponsoring the study

Insurance - The University of Dundee will obtain and hold a policy of Public Liability Insurance for legal liabilities arising from the study.

Tayside health Board will maintain its membership of the Clinical Negligence and Other Risks Insurance Scheme (CNORIS), which covers the legal liability of Tayside in relation to the study.

Where the study involves University of Dundee staff undertaking clinical research on NHS patients, such staff will hold honorary contracts with Tayside Health Board, which means the will have cover under Tayside's membership of the CNORIS scheme.

Indemnity - The Co-Sponsors do not provide study participants with indemnity in relation to participation in the study but have insurance for legal liability as described above.

Amendments

The PI/CI will seek approval for any amendments to the protocol or other study documents from the Sponsor, UREC and NHS R&D Offices. Amendments to the protocol or other study docs will not be implemented without these approvals.
In the event that a CI needs to deviate from the protocol, the nature and the reasons for the deviation will be recorded in the study master file (SMF) documented and submitted to the Sponsor. If this necessitates a subsequent protocol amendment, this will be submitted to the Sponsor for approval and then to the appropriate REC and lead NHS R&D office for review and approval..
In the event that a serious breach of GCP is suspected, this will be reported to the Sponsor immediately using the form "Notification to Sponsor of Serious Breach or Serious Deviation".

End of Study

There are three significant points during the process of this study:

(1) the end of data collection, which is determined when data saturation is achieved;
(2) completion of data analysis and interpretation; and
(3) submission of the study final report.

The end of study is defined as the end of data analysis and interpretation The Sponsor, and/ or CI have the right at any time to terminate the study for clinical or administrative reasons. The end of the study will be reported to the Sponsor and REC within 90 days, or 15 days if the study is terminated prematurely. A summary report of the study will be provided to the Sponsor and REC within 1 year of the end of the study.

Dissemination

The study findings will be available on request. Findings will be presented at organised events as well as in scientific conferences. A publication plan will be developed with the aim to present the main study findings in a relevant peer reviewed journal.

Authorisation policy

Ownership of the data arising from this study resides with the study team and their respective employers.

Publication

The study report will be used for publication and presentation at scientific meetings. Investigators have the right to published orally or in writing the results. Summaries of results will also be made available to investigators for dissemination within their clinical areas (where appropriate and accordance to

their discretion). The study will form part of the PI's doctoral thesis which will be published in line with University procedures.

6. References

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Appendix 6 NHS Tayside and Grampian approval letter

NHS Tayside

04 December 2018

Professor Nicola Innes
Professor of Paediatric Dentistry/Associate Dean for Learning & Teaching
Dundee Dental Hospital and School
Park Place
Dundee
DD1 4HR

Dear Professor Innes,

R&D MANAGEMENT APPROVAL – TAYSIDE

Title: Dental Care Professionals' views of silver diamine fluoride for the management of carious lesions in children: a qualitative study.

Chief Investigator: Professor Nicola Innes

Principal Investigator/Local Collaborator: Mr Nassar Seifo

Tayside Ref: 2018DE03 **NRS Ref: NRS18/252305** **IRAS ID: 252305**

REC Ref: N/A

Sponsor: University of Dundee and NHS Tayside

Funder: Unfunded

Many thanks for your application to carry out the above project here in NHS Tayside. I am pleased to confirm that the project documentation (as outlined below) has been reviewed, registered and Management Approval has been granted for the study to proceed locally in Tayside.

Approval is granted on the following conditions:-

- ALL Research must be carried out in compliance with the Research Governance Framework for Health & Community Care, Health & Safety Regulations, data protection principles, statutory legislation and in accordance with Good Clinical Practice (GCP).
- All amendments to be notified to TASC R&D Office via the correct amendment pathway. Either direct to the R&D Office or via the Lead Co-ordinating Centre depending on how the study is set up.
- All local researchers must hold either a Substantive Contract, Honorary Research Contract, Honorary Clinical Contract or Letter of Access with NHS Tayside where required (http://www.nihr.ac.uk/about-us/CCF/policy-and-standards/research-passports.htm).
- TASC R&D Office to be informed of change in Principal Investigator, Chief Investigator or any additional research personnel locally.

- Notification to TASC R&D Office of any change in funding.
- As custodian of the information collated during this research project you are responsible for ensuring the security of all personal information collected in line with NHS Scotland IT Security Policies, until destruction of this data.
- All eligible and adopted studies will be added to the Central Portfolio Management System (CPMS). Recruitment figures for eligible and adopted studies must be recorded onto the Portfolio every month. This is the responsibility of the lead UK site. If you are the lead, or only UK site, we can provide help or advice with this. For information, contact the local Portfolio team at tascportfolio.tayside@nhs.net.
- Annual reports are required to be submitted to TASC R&D Office with the first report due 12 months from date of issue of this management approval letter and at yearly intervals until completion of the study.
- Notification of early termination within 15 days or End of Trial within 90 days followed by End of Trial Report within 1 year to TASC R&D Office.
- You may be required to assist with and provide information in regard to audit and monitoring of study.

Please note you are required to adhere to the conditions, if not, NHS management approval may be withdrawn for the study.

Approved Documents

Document	Version	Date
SREC Approval Letter		**31/08/18**
Reply Slip	**1.0**	**30/07/18**
Interview Topic Guide	**1.0**	**30/07/18**
Informed Consent Form (Face to Face)	**1.0**	**30/07/18**
Over the Phone Interview Consent Form	**1.0**	**30/07/18**
Protocol	**1.0**	**30/07/18**
Participant Information Sheet	**1.1**	**14/08/18**

May I take this opportunity to wish you every success with your project.

Please do not hesitate to contact TASC R&D Office should you require further assistance.

Yours sincerely

Elizabeth Coote
Head of Non-Commercial Research Services

TAyside medical Science **C**entre (TASC)
Ninewells Hospital & Medical School
TASC Research & Development Office
Residency Block, Level 3
George Pirie Way
Dundee DD1 9SY

cc: Nassar Seifo, Dundee
Research Monitor

Sponsor: NHS Tayside / University of Dundee

Appendix 7 Participants information sheet for the qualitative study with DPs

Participant Information Sheet

Study title: Dental Care Professionals' views of silver diamine fluoride for the management of carious lesions in children: a qualitative study

Study researchers*:* Nassar Seifo

We would like to invite you to take part in this research study

We are asking you to consider taking part in a research study that forms part of my PhD project within the School of Dentistry at the University of Dundee under supervision of Prof Nicola Innes. We are conducting a research study at University of Dundee to explore children's, parent/carers' and Dental Care Professionals' (including dentists, dental therapists and dental nurses) views on Silver Diamine Fluoride (SDF). You may have heard of SDF as it has recently become available in the UK. SDF is used to manage dental caries by applying the solution to active carious lesions to arrest them.

To understand how best to improve training and teaching of new techniques like SDF we need to understand the thoughts and perspectives of Dental Care Professionals, like yourself, on treating children patients especially with regard to SDF.

Your responses to the questions will be made anonymous and kept confidential. Each interview will be assigned a number code to ensure that personal identifiers are not revealed during the analysis and write up of findings.

Your participation will be a valuable addition to our research and may help to inform future practice. Please take time to read the enclosed information sheet carefully and think about whether or not you would like to take part.

This study is being sponsored by the University of Dundee and NHS Tayside. It is being funded by the University of Dundee. The study has been organised by Professor Nicola Innes.

What is the project's purpose?

This research project aims to explore what Dental Care Professionals think of Silver Diamine Fluoride (SDF) for the management of carious lesions in primary teeth.

Biannual SDF application arrests active caries and has been found to be useful especially in uncooperative children or children with special needs. However, one disadvantage of SDF is that carious lesions will be stained black permanently. This study will explore your thoughts on the use of SDF as a management option for carious lesions in children's primary teeth, whether your previous experience has an impact on your preferred treatment approaches, and your perspectives of parent/guardians' preferences.

Do I have to take part?

No. It is up to you to decide. Participation in this study is entirely voluntary and you are free to refuse to take part or to withdraw from the study at any time without having to give a reason and without this affecting your future medical care or your relationship with medical or nursing staff looking after you.

What will happen if I take part?

If you indicate to us that you are interested in taking part, you will be contacted by one of the researchers to arrange for a time for an interview. This can be face-to-face or over the telephone.

If you are based in Grampian, they will be phone-interviews. If you are based in Tayside, if you are within Dundee, they might be an arrangement to visit you at the clinic if they wish, otherwise they will be phone-interviews

The interview will be audio recorded with a digital voice recorded but your views will be kept confidential – all data will be anonymised.

Prior to the interview, consent will be explained and obtained. For face-face interviews, the consent will be taken in person, while for over-the-phone interviews the consent will be obtained via phone and it will be audio recorded.

If you would like to participate, please write your email or phone number on the reply slip below and let us know the best times to contact you so that we can get in touch to arrange a time for an interview.

What will happen with the information collected about me?

Identifiable information about you and the information collected about you during the trial/study will be stored by the University of Dundee. Only specified members of the research team will have access to this information.

Your identifiable information and coded study information/your anonymised coded study information will be stored securely on a password-protected database(s) in the University of Dundee. Specified members of the data management team will also have access to your identifiable information to manage your information and maintain the database.

Your information will be kept securely for five years after the end of the study/trial. After five years it will be destroyed/ or your identifiable information will be removed and the rest of the information will be kept for research purposes.

Information which identifies you will not be published or shared. Your study information with any information which identifies you removed may be shared with other researchers in the UK.

What are the possible disadvantages and risks of taking part?

There are no known risks to you from taking part in the study. You don’t have to tell us anything you don’t want to. There are no anticipated disadvantages or discomfort.

What are the possible benefits of taking part?

Taking part in the study is likely to inform future practice, it is hoped that this work will help find out more about whether DCPs think this is a good treatment for carious lesions in primary teeth instead of conventional treatment and how we might tailor training, teaching and information materials for DCPs, on the use of SDF.

What if something goes wrong?

If you have any concerns about your participation in the study, you have the right to raise your concern with a researcher involved in conducting the study or a doctor involved in your care.

If you have a complaint about your participation in the study, you should first talk to a researcher involved in the study. However, you have the right to raise a formal complaint. You can make a complaint to a senior member of the research team or to the Complaints Officer for NHS Tayside or Grampian.

NHS Tayside Complaints and Feedback Team
NHS Tayside
Ninewells Hospital
Dundee DD1 9SY
Freephone: 0800 027 5507
Email: feedback.tayside@nhs.net
NHS Grampian Complaints and feedback Team

NHS Grampian Feedback Service
Summerfield House
2 Eday Road
Aberdeen
AB15 6RE
Tel: 0345 337 6338
E-mail: nhsgrampian.feedback@nhs.net

In the event that you think you have suffered harm as a result of your participation in the/study there are no automatic financial compensation arrangements. However, you may have the right to make a claim for compensation. Where you wish to make a claim, you should consider seeking independent legal advice, but you may have to pay for your legal costs.

Insurance

The University of Dundee and Tayside Health Board are Co-Sponsoring the study. The University of Dundee maintains a policy of public liability insurance which provides legal liability cover in respect of damages, costs and expenses arising out of claims.

Tayside Health Board is a member of the NHS Scotland Clinical Negligence and Other Risks Insurance Scheme (CNORIS) which provides legal liability cover of NHS Tayside in relation to the study.

As the study involves University of Dundee staff undertaking clinical research on NHS Tayside patients, such staff hold honorary contracts with Tayside Health Board which means they will have cover under Tayside's membership of the CNORIS scheme.

Other Scottish Health Boards are participating as study sites and they also maintain membership of CNORIS to cover their liability in relation to their conduct of the study.

Who has reviewed this study?

This study has been reviewed and approved by University Research Ethics Committee who are responsible for reviewing research which is conducted in humans and who has raised no objections. The Research Ethics committee does not have any objections to this study going ahead.

Contact details for further information.

Nassar Seifo, Dundee Dental School, University of Dundee, UK. Tel: +44 (0)739 7723 222, email: nseifo@dundee.ac.uk (PhD Candidate and Researcher)

Professor Nicola Innes, Dundee Dental School, University of Dundee, UK. Tel: +44 (0)1382 381631, email: n.p.innes@dundee.ac.uk (Professor of Paediatric Dentistry and Associate Dean for Learning and Teaching)

Thanks for taking time to read this information and for considering participating in this study.
If you would like more information or want to ask questions about the study, please contact the study team using the contact details above.

Appendix 8 Reply slip for the qualitative study with DPs

Reply slip

Study title: Dental Care Professionals' views of silver diamine fluoride for the management of carious lesions in children: a qualitative study

Chief Investigator: Professor Nicola Innes

Principal Investigator: Nassar Seifo

For more information or to take part in the study, please contact Nassar Seifo in the research team by telephone, email or post.

☎ Tel 07397723222

Email nseifo@dundee.ac.uk

Post **Please complete the form below and return it in the Stamped Self-addressed envelope**

Yes, I would like to find out more about the study. Please contact me.

Name ……

Profession: Dentist / Dental hygienist/ Dental nurse/ Dental therapist / Vocational Dental Practitioner **(please circle)**

My contact details:	Best way to contact me (please tick):	Best time to call:
Day time number: ……	☐	……
Mobile number: ……	☐	……
Email address: ……	☐	……

If you would like to contact the research team instead of posting the reply slip, please find contacts details attached in the information sheet

Appendix 9 Informed consent forms for the qualitative study with DPs

University of Dundee

NHS Tayside SDPBRN

INFORMED CONSENT FORM

Participant Identification Number:

Title of Study: Dental Care Professionals' views of silver diamine fluoride for the management of carious lesions in children: a qualitative study

Name of the Researcher: Nassar Seifo

Sponsors: University of Dundee and NHS Tayside

Please initial box

1. I confirm that I have read the information sheet/leaflet dated..... (version.....) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. ☐
3. Any data collected up to the point of withdrawal from the research will be kept anonymously and used for the research purposes. This will include research publications. ☐
4. I understand that personal data about me and research data collected during the study will be stored by the University of Dundee ☐
5. I understand that relevant sections of my medical records and data collected during the study, may be looked at by the Researcher and/or research team, the Sponsors or regulatory authorities where it is relevant to my taking part in this research. I give permission for the Researcher and/or research team, the Sponsors and regulators to have access to my records and data. ☐
6. I understand that my research data collected by the Researcher and/or research team in this study may be used to support other research in the future, and may be shared anonymously with other researchers or collaborators, including commercial organisations. ☐
7. I understand that the study involves one-to-one interview which includes me and the researcher. ☐
8. I understand that the interviews will be audio recorded, anonymised and typed up. ☐
9. I agree to give my phone number and to be re-contacted briefly via a phone call for clarifying some aspects of my study interview. ☐
10. I agree to take part in the above study. ☐

Name of Participant (CAPS)	Date	Signature
Name of Person taking consent (CAPS)	Date	Signature

1 for participant, 1 to be kept in medical records and 1 for study file.

University of Dundee

NHS Tayside SDPBRN

Over-the-phone interviews consent form

Participant Identification Number:

Title of Study: Dental Care Professionals' views of silver diamine fluoride for the management of carious lesions in children: a qualitative study

Name of the Researcher: Nassar Seifo

Sponsors: University of Dundee and NHS Tayside

Interviewer will tick the box

1. I confirm that I have read the information sheet/leaflet dated..... (version.....) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. ☐
3. Any data collected up to the point of withdrawal from the research will be kept anonymously and used for the research purposes. This will include research publications. ☐
4. I understand that personal data about me and research data collected during the study will be stored by the University of Dundee ☐
5. I understand that relevant sections of my medical records and data collected during the study, may be looked at by the Researcher and/or research team, the Sponsors or regulatory authorities where it is relevant to my taking part in this research. I give permission for the Researcher and/or research team, the Sponsors and regulators to have access to my records and data. ☐
6. I understand that my research data collected by the Researcher and/or research team in this study may be used to support other research in the future, and may be shared anonymously with other researchers or collaborators, including commercial organisations. ☐
7. I understand that the study involves one-to-one interview which includes me and the researcher. ☐
8. I understand that the interviews will be audio recorded, anonymised and typed up. ☐
9. I agree to give my phone number and to be re-contacted briefly via a phone call for clarifying some aspects of my study interview. ☐
10. I agree to take part in the above study. ☐

_____	_____	
Name of Participant (CAPS)	Date	
_____	_____	_____
Name of Person taking consent (CAPS)	Date	Signature

1 for participant, 1 to be kept in medical records and 1 for study file.

Appendix 10 Topic guide for the qualitative study with DPs

Study title: Dental Care Professionals' views of silver diamine fluoride for the management of carious lesions in children: a qualitative study

INTERVIEW TOPIC GUIDE

Introduction

- *My name is Nassar Seifo, I am a PhD student at Dundee Dental School and Hospital. Thank you for participating in this interview.*

Previous experience

Firstly, can I just find out a little bit about you ….

- *What is your role in the practice/clinic?*
- *How long have you been qualified?*
- *How often do you see children in the clinic?*
- *How do you feel about treating children?*
- *Tell me about your favourite aspect of treating children?*
- *Tell me about the aspect of treating children that you find most challenging?*
- *Can you describe to me what you do when you have to provide treatment for a child patient who is stressed or scared?*
- *How do you think that your previous experiences with child patients have influenced your treatment planning?*

Silver Diamine Fluoride

- *What do you know about SDF?*
- *Have you tried applying SDF? If yes, could you tell me more about it?*
- Are you aware of any colleagues using? Did you provide any feedback?
- *What advantages do you think SDF has over traditional treatment?*
- *What do you think the barriers would be to you using it for carious lesions in primary teeth?*
- *If you had it available to you in practice, what do you think might help you to use it for primary teeth?*
- *For which cases might you consider SDF instead of the current treatments you have available?* Why? What factors would you take into consideration?

Parents/carers preferences

- What do you think concerns parents when it comes to their child's dental treatment?
- What do you think parents see as the benefits of having their child have dental treatment?
- How do you think parents would feel about offering SDF and telling them it would make the decayed part of the tooth black?
- What do you think children would feel about having a black tooth (front/back)?

Any other comments/thoughts regarding the use of SDF for the management of carious lesions in children or any other related issues you would like to raise?

Thank them for their time and participation.

Appendix 11 Parents/Carers' and children's views of silver diamine fluoride for the management of carious lesions in children: a multi-methods study (Protocol)

Nassar Seifo, Heather Cassie, John Radford and Nicola Innes

1. Background

There have been significant advances in dental care over the last few decades. However, dental caries (tooth decay) is still one of the most prevalent chronic diseases affecting people from different countries (35% of permanent teeth and 9% of primary teeth have untreated dental carious lesions) and across all age groups (Marcenes et al. 2013).
Conventional dental treatment for managing carious lesions is expensive. In addition, it may not be possible in certain groups such as children, adults and children with dental anxiety or those with disabilities. Current research suggests that dental caries should not always be managed using a traditional "drill and fill" approach but instead by using less invasive and more cost-effective methods (Schwendicke 2017). One method found to be effective in carious lesion management is silver diamine fluoride (SDF). SDF arrests the lesion's progression hence reducing associated pain and infection (Chibinski et al. 2017; Gao et al. 2016).
One side effect of SDF is that the carious lesion becomes stained black after application. However, it has been suggested that parents may view this discoloration as a positive indication that the treatment has been effective (Horst et al. 2016). In addition, a recent survey-based study found that staining on posterior teeth was more acceptable than staining on anterior teeth and although staining on anterior teeth was undesirable, most parents preferred this option to advanced behavioural techniques such as sedation or general anaesthesia (Crystal et al. 2017). It is not clear yet where the threshold for accepting this treatment and the undesirable effect of staining lies for parents/carers and whether there are any other barriers or facilitators to using SDF. This therefore presents an opportunity for further exploration to improve treatment decision making.

2. Rationale

There is evidence that SDF can be used to arrest dental caries but during this process it causes black discolouration of the carious lesions. SDF has recently become available for use in the UK, presenting an opportunity to explore its acceptability for managing dental carious lesions in primary teeth from both the children's and parents'/carers' perspective. There is an increasing emphasis on capturing the views of children within health services research to ensure that the treatments they are offered and their views on treatment outcomes are heard and addressed (Marshman *et al*., 2015) and, this study will address this by exploring the acceptability as well as the potential barriers and enablers to the use of SDF as a treatment approach for the children and their parents/carers. The results will contribute towards the implementation of this intervention into dental practice.

3. Research question/aim(s)

Study aims

- To explore parent/carers' perspectives, on treatment options to manage dental carious lesions in children, with a focus on SDF.
- To explore children's perspectives on treatment options to manage their dental carious lesions, with a focus on SDF.

Objectives

To explore with parents/carers, for the carious primary dentition:
- the acceptability and barriers and enablers to the use of SDF;
- treatment preferences;
- factors that influence their decision making around treatment options;
- priorities placed on the management options;
- whether parent/carers' decision is impacted by the child's previous dental experience.

To explore with children, for carious primary dentition:
- their view and acceptability of SDF as a treatment option;
- their previous dental experience.

4. Methods

Study design

A multi-methods study incorporating
(1) A questionnaire-based survey
(2) Semi-structured interviews

Setting

Dundee Dental Hospital and School (DDH&S).

Participants

Inclusion criteria
- Parents/carers, and their children (aged 4 to 12 years, at the time of consent) who come to DDH&S;
- English speakers of any ethnicity.
- Able to provide consent

For the purposes of this protocol, the remainder of this document will refer simply to 'parents', as being anyone with the legal authority to consent to a child participating in this study.

Exclusion criteria
Parents with children aged outside the stated age range, non-English speakers or unable to provide consent.

Recruitment

(1) Questionnaire
A convenience sampling approach will be used to recruit participants from the Child Dental Health Clinic in DDH&S. Based on the number of patients attending the clinic every day, it is anticipated that up to 120 parents-children may be recruited.

(2) *Interviews*
A purposive sampling framework will be used, based on eligibility criteria developed according to the research objectives and questions, to ensure that the sample is heterogenous in terms of gender and age. Data collection will be carried out until saturation is reached i.e. when no new themes, categories or explanations are emerging from the data. An initial recruitment target of 20 participants per group (20 parents and 20 children) will be sought but this will be guided by the data obtained during the interviews.

The study sample will be identified and recruited from those attending the Child Dental Health Clinic in DDH&S. Potential participants will be given a minimum of 24 hours to think about their participation in the study. The researcher will identify potential participants at the beginning of each day from the list of children attending the Clinic. At the end of the child's appointment, the parent will be approached by one of the Dental Care Professionals (DCPs) at clinic who will explain the study and that there are two parts of the study; one includes a questionnaire only and the other includes an interview and a questionnaire. If they showed interest in a part of the study, the DCPs will hand them a specific information pack based on whichever part they are interested in taking part in.

- The questionnaire part of the information pack includes the participant's information sheet (PIS) for the parents that describes the study in detail, the questionnaire and a freepost envelope.
- The interview/questionnaire part of the information pack includes the PIS for parents that describes the study in detail, the PIS for children that is tailored for the child's age (preschool, P1-P3; and P4-P7), a reply slip to provide the research team with their response, contact details and the best time to be contacted and a freepost envelope.

Parents interested in participating will have the opportunity to call the PI or CI if they have further queries about the study on the telephone number provided in the contact details section of the PIS.

- Participants who decide to take part in the questionnaire part of the study will return the completed questionnaire either by post using the freepost envelope or by putting it into the box located on the clinic at their next visit.

- Participants who decide to take part in the interview/questionnaire part of the study can put the reply slip into a box at the reception in Child Dental Health Clinic at their next visit or post it using the freepost envelope provided. The PI will carry out pre-screening for eligibility either by telephone when the parent calls or when they call them back if they have placed contact details in the recruitment box on the clinic. The PI will also discuss the study, answer any questions and arrange a time and place for the interview appointment if the parent wishes to participate. Participants will be able to discuss their involvement in the study with any of the clinicians on the Child Dental Health Clinic they wish (all staff are aware of the study and what it involves). Recruitment will cease once data saturation is achieved. Participants in the questionnaire/interview part will receive a £10 Love2Shop voucher to thank them for taking part.

Data Collection

(1) Questionnaire

The questionnaire will explore the priority placed on the management of dental caries when considering all treatment options and what parents think of their child's previous visits to the dentists. At the end of the questionnaire there is a question about what the child thinks of their previous visits to see a dentist. The parent can complete this question with the child, or the child, if old enough, can circle the answer by themselves.

The questionnaire was adapted from a similar study conducted in the United States which refining it to be more suitable for the population in the UK and more related to our study aims(Crystal et al. 2017).

The questionnaire to be piloted to test content validity with a small group of similar people to the targeted sample (around 5-10 parents-children).

(2) Interviews

Face-to-face audio-recorded semi-structured interviews, using open-ended questions and probing will be conducted by the PI. Interviews will last no longer than 60 minutes (parent interview ≤ 45 mins + child interview ≤ 15 mins). The parent will be interviewed first, then the child, with both being together in the room for both interviews.

A topic guide, informed by the literature, will be used as a broad framework for the interviews. Prior to the interview, potential participants will be given the opportunity to ask any questions and if they are happy to take part, a written informed consent will be obtained before the start of the interview. The consent process will be conducted following TASC SOP07 (Tayside Academic Health Science Partnership Standard Operating Procedure).

Interviews with parents and their children will be conducted in a convenient venue at the DDH&S. Questions will explore the acceptability and enablers of, as well as barriers to the use of SDF, factors that influence their decision-making regarding the treatment options, and whether previous dental experience for the child has an impact on parents' decisions. Questions for children will explore their views toward SDF treatment and what they think of their previous visits to see a dentist.

Interview schedules have been piloted with parents and children prior to starting the study to ensure they are clear to the target populations. Revisions to the schedules have been made as appropriate. All interviews with be audio recorded with participant consent.

Data Analysis

(1) Questionnaire

Analysis will be conducted by the PI using Statistical Package for the Social Sciences (SPSS) software which is a comprehensive system for analysing data. Descriptive statistics will be used to describe the basic features of the data and provide simple summaries about the sample and check the distribution, central tendency and dispersion.

Analysis will be carried out on a password protected computer at the University of Dundee.

- **Missing data**

If a question is unanswered, the researcher, when entering data into a survey analysis program, will record a missing value or enter a code for, for example, 'Not applicable' or 'Refused to answer'

- **Data assembling**

Data assembly means gathering together all the checked, edited and coded questionnaires, and entering the values for each variable for each case into data analysis software. This is usually achieved in a framework of rows and columns for storing the data called a data matrix. Data will be assembled first into a spreadsheet like Excel before exporting to SPSS.

(2) Interviews

Analysis will be conducted by the PI using a framework approach to qualitative data analysis. This is a matrix-based method, using a thematic framework to organise and classify data according to key issues, concepts and emerging themes (Ritchie and Spencer, 1994). Data management will be facilitated using NVivo software, which is produced by QSR International (https://www.qsrinternational.com/). All interviews will be recorded and transcribed in full; a sample of interviews will be transcribed by the PI and the rest will be transcribed via transcription service (NJC Secretarial). However, all identifiable data will be anonymised before they are transferred to third party service for transcription. Audio recordings and transcripts will be uploaded into NVivo to facilitate

data management. Analysis will be carried out on a password protected computer at the University of Dundee.

The five stages of data analysis using the framework approach will then be conducted;

1- **Familiarisation:** This involves the researcher re-listening to all interview recordings and reading through the transcripts and any notes taken at the time of the interviews. This will provide the researcher with an opportunity to articulate and note down some initial thoughts and themes.
2- **Identifying a thematic framework:** During this process the researcher can draw upon a priori issues and, therefore, the initial framework is often largely descriptive and rooted within these a priori issues.
3- **Indexing:** This is where the data is applied to framework headings and involves identifying sections of the text that are associated with these. This process will inform the development of sub-themes. It may be that sections of the text are aligned to two or more themes and when new sub-themes emerge, the researcher will revisit previous transcripts to establish if they are common themes. This process will ensure saturation of themes.
4- **Charting:** This involves applying the data from the individual transcripts to the index, this information is then extracted from its original context and rearranged according to the key themes emerging from the data as a whole. This will allow comparisons to be made across participants e.g. parents, children, different healthcare professional roles.
5- **Mapping and interpretation:** The final stage will draw together the key characteristics of the data and interpret it as a whole. This will involve comparing and contrasting experiences and perceptions and explore similarities and differences across the data to provide explanations.

The Consolidated Criteria for Reporting Qualitative Research (COREQ) will guide reporting of the data (Tong el al., 2007).

5. Ethical and Regulatory Considerations

Research Governance

For the duration of the study, all paperwork with study data will be stored securely in a locked cabinet within University of Dundee, only accessible by the main investigators. Digital, anonymised data in the form of interview recordings and transcriptions will be stored in an encrypted and password protected University of Dundee secured database. Data will be available and ready for an audit if required. All data will be archived and stored securely for five years after completion of the project in line with University of Dundee policy.

Consent

Prior to interview, the PI will discuss the study with the participants and they will have the chance to ask any questions. The written consent will be read, explained and discussed with all parents who agree to take part in the study to make sure they understand it before signing. Two copies of signed consent by the participant must be provided before commencement. One copy will be given to the participant and one for the study file. The consent will include critical and important actions that may be carried out during the interview (voice recording, details on interview nature, purpose of the interview, etc.).

The child assent process will involve speaking to the child with the parent present and, similar to other studies, this will be done in the side room of the clinic where there is no dental chair but with the door open. The assent process will involve taking time to explain to the child about what will happen in the study, why the is it being done and what the interview is about. It will also involve answering any questions the child may ask about the study. They will be told that if they wish they can withdraw any time without giving reason and nobody will know about them taking part in the study apart from their carers. A simplified language considering the child's age will be used, so that every child would understand. We will ask the parents to help with explaining to the child as they will be familiar with the language the child knows and what level of understanding they have around talking to people about what they think.
It is usually inappropriate to ask very young children (e.g. under 5's) to sign an assent form, however their views will be considered. An informed judgment to determine when seeking assent is appropriate will be informed by discussion with the parent; the age of a child can be taken as a guide. The child's developmental stage should also be considered.

For the questionnaire, completing and returning the questionnaire will be considered as implied consent.

Withdrawal procedure

Participants have the right to withdraw at any stage of the study without giving any reason. If a participant withdraws, we will ask if they will allow us to continue to use the data already collected and if they do not wish this, their data will be deleted. All data collected prior to their withdrawal will be kept confidential and will be anonymised in the same way as for other participants.

Assessment and management of risk

If a participant feels distressed or uncomfortable during an interview, the interview will be terminated immediately, and voice recording will be stopped. A supportive conversation will take place and the participant will be asked if they wish to continue the interview or terminate it. The PI has attended a session about child protection, and how to listen carefully to the messages the child sends, at the School of Education and Social Work, University of Dundee.

Data Management System

Data management will be conducted in compliance with TASC SOPs on Data Management, including TASC SOP53 Data Management Systems in Clinical Research. The data management system (DMS) will be NVivo, Excel and SPSS, as approved by Sponsor.
The DMS will be based on the protocol and individual requirements of the investigators. The Study Master file will collect only information that is required to meet the aims of the study and to ensure the eligibility and safety of the participant. The study database will be compliant with TASC SOP53 Data Management Systems in Clinical Research.
The database is managed in line with all applicable principles of medical confidentiality and data laws. The Data Controller will be the University of Dundee and the Data Custodian will be the CI.
Database lock will be conducted in compliance with TASC SOP32 Locking Clinical Study Databases.

Research Ethics Committee (REC) review and reports

The study will be conducted in accordance with the principles of Good Clinical Practice. In addition to sponsorship approval, ethical favourable opinion will be obtained from the appropriate REC, and appropriate NHS Tayside R&D approval will be obtained prior to commencement of the study.

Data protection and patient confidentiality

The CI and trial staff will comply with all applicable medical confidentiality and data protection principles and laws with regard to the collection, storage, processing and disclosure of personal data.
The CI and trial staff will also adhere to the NHS Scotland Code of Practice on Protecting Participant Confidentiality or equivalent.
All trial records and personal data will be managed in a manner designed to maintain participant confidentiality. All records, electronic or paper, will be kept in a secure storage area with access limited to appropriate trial staff only. Computers used to collate personal data will have limited access measures via user names and passwords.
Personal data concerning health will not be released except as necessary for research purposes including monitoring and auditing by the Sponsor, its designee or regulatory authorities providing that suitable and specific measures to safeguard the rights and interests of participants are in place.
The CI and trial staff will not disclose or use for any purpose other than performance of the trial, any personal data, record, or other unpublished, confidential information disclosed by those individuals for the purpose of the trial. Prior written agreement from the Sponsor will be required for the disclosure of any said confidential information to other parties.
Access to collated personal data relating to participants will be restricted to the CI and appropriate delegated trial staff.
Where personal data requires to be transferred, an appropriate Data Transfer Agreement will be put in place.
Published results will not contain any personal data that could allow identification of individual participants.

Insurance and Indemnity

The University of Dundee and Tayside Health board are Co-Sponsoring the study.

Insurance - The University of Dundee will obtain and hold a policy of Public Liability Insurance for legal liabilities arising from the study.
Tayside Health Board will maintain its membership of the Clinical Negligence and Other Risks Insurance Scheme (CNORIS), which covers the legal liability of Tayside in relation to the study.
Where the study involves University of Dundee staff undertaking clinical research on NHS patients, such staff will hold honorary contracts with Tayside Health Board, which means the will have cover under Tayside's membership of the CNORIS scheme.

Indemnity - The Co-Sponsors do not provide study participants with indemnity in relation to participation in the study but have insurance for legal liability as described above.

Protocol Amendments, deviations and breaches

Refer to TASC SOP 30: Substantial Amendments in Clinical Research
The CI will seek approval for any amendments to the Protocol or other study documents from the Sponsor, REC and NHS R&D Office(s). Amendments to the protocol or other study docs will not be implemented without these approvals.
In the event that a CI needs to deviate from the protocol, the nature of and reasons for the deviation will be recorded in the CRF, documented and submitted to the Sponsor. If this necessitates a subsequent protocol amendment, this will be submitted to the Sponsor for approval and then to the appropriate REC and lead NHS R&D Office for review and approval.
In the event that a serious breach of GCP or protocol is suspected, this will be reported to the Sponsor Governance Office immediately.

Study Record Retention

Archiving of study documents will be for five years after the end of study.

End of Study

There are three significant points during the process of this study:

1- the end of data collection, which is determined when data saturation is achieved;
2- completion of data analysis and interpretation; and
3- submission of the study final report.

The end of study is defined as the end of data analysis and interpretation The Sponsor, and/ or CI have the right at any time to terminate the study for clinical or administrative reasons.

The end of the study will be reported to the Sponsor and REC within 90 days, or 15 days if the study is terminated prematurely.

A summary report of the study will be provided to the Sponsor and REC within 1 year of the end of the study.

Dissemination

The study findings will be available on request. Findings will be presented at organised events as well as in scientific conferences. A publication plan will be developed with the aim to present the main study findings in a relevant peer reviewed journal.

Authorship policy

Ownership of the data arising from this study resides with the study team and their respective employers. On completion of the study, the study data will be analysed and tabulated, and a clinical study report will be prepared.

Publication

The study report will be used for publication and presentation at scientific meetings. Investigators have the right to published orally or in writing the results.

Summaries of results will also be made available to investigators for dissemination within their clinical areas (where appropriate and accordance to their discretion). The study will form part of the PI's doctoral thesis which will be published in line with University procedures.

Peer review

This project has been designed and the protocol iteratively reviewed by three experienced reviewers who are the PI's PhD supervisory team. The project is the partial fulfilment of a PhD in Dentistry and will be examined through Viva Voce examination. The PI's work will be examined, and peer reviewed by an internal examiner from University of Dundee as well as an external examiner from another University Institution.

6. References

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Horst JA, Ellenikiotis H, Milgrom PM, Committee USCA. 2016. Ucsf protocol for caries arrest using silver diamine fluoride: Rationale, indications, and consent. Journal of the California Dental Association. 44(1):16.

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Appendix 12 Research Ethics Committee favourable opinion letter for the multi-methods study with parents and children

NHS SCOTLAND

East of Scotland Research Ethics Service *(EoSRES)* **Research Ethics Service**

TAyside medical Science Centre
Residency Block Level 3
George Pirie Way
Ninewells Hospital and Medical School
Dundee DD1 9SY

Professor Nicola P T Innes
Professor of Paediatric Dentistry
School of Dentistry
University of Dundee
Dundee Dental Hospital & School
Park Place
Dundee
DD1 4HN

Date: 14 May 2019
Your Ref:
Our Ref: LR/19/ES/0042
Enquiries to: Mrs Lorraine Reilly
Direct Line: 01382 383878
Email: eosres.tayside@nhs.net

Dear Professor Innes

Study Title:	**Parents/Carers' and children's views of silver diamine fluoride for the management of carious lesions in children: a multi-methods study**
REC reference:	**19/ES/0042**
Protocol number:	**1-002-19**
IRAS project ID:	**254563**

Thank you for your letter received on 13 May 2019, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Vice-chair, together with other named members as appropriate.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to make a request to postpone publication, please contact hra.studyregistration@nhs.net outlining the reasons for your request.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Conditions of the favourable opinion

The REC favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission must be obtained from each host organisation prior to the start of the study at the site concerned.

disability confident EMPLOYER

Management permission should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements. Each NHS organisation must confirm through the signing of agreements and/or other documents that it has given permission for the research to proceed (except where explicitly specified otherwise). Guidance on applying for HRA and HCRW Approval (England and Wales)/ NHS permission for research is available in the Integrated Research Application System, at www.hra.nhs.uk or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of management permissions from host organisations

Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database within 6 weeks of recruitment of the first participant (for medical device studies, within the timeline determined by the current registration and publication trees).

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g. when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non-clinical trials this is not currently mandatory.

If a sponsor wishes to request a deferral for study registration within the required timeframe, they should contact hra.studyregistration@nhs.net. The expectation is that all clinical trials will be registered, however, in exceptional circumstances non registration may be permissible with prior agreement from the HRA. Guidance on where to register is provided on the HRA website.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Ethical review of research sites

NHS sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Non-NHS sites

The Committee has not yet completed any site-specific assessment (SSA) for the non-NHS research site(s) taking part in this study. The favourable opinion does not therefore apply to any non-NHS site at present. We will write to you again as soon as an SSA application(s) has been reviewed. In the meantime no study procedures should be initiated at non-NHS sites.

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	Version	Date
Interview schedules or topic guides for participants [Topic Guide]	1.0	11 February 2019
IRAS Application Form [IRAS_Form_18032019]		18 March 2019
IRAS Checklist XML [Checklist_18032019]		18 March 2019
IRAS Checklist XML [Checklist_13052019]		13 May 2019
Letter from sponsor [Sponsor letter and Insurance cover]		05 March 2019
Non-validated questionnaire [Questionnaire (highlighted changes)]	1.1	08 May 2019
Other [Response to the REC]		
Participant consent form [Assent form children]	1.0	11 February 2019
Participant consent form [ICF Parents (highlighted changes)]	1.1	08 May 2019
Participant information sheet (PIS) [Reply Slip Parents]	1.0	11 February 2019
Participant information sheet (PIS) [PIS Parents Interview+questionnaire (highlighted changes)]	1.1	08 May 2019
Participant information sheet (PIS) [PIS Questionnaire (highlighted changes)]	1.1	08 May 2019
Participant information sheet (PIS) [PIS preschool (highlighted changes)]	1.1	08 May 2019
Participant information sheet (PIS) [PIS P1-P3 (highlighted changes)]	1.1	08 May 2019
Participant information sheet (PIS) [PIS P4-P7]	1.1	08 May 2019
Research protocol or project proposal [Protocol (highlighted changes)]	1.1	08 May 2019
Summary CV for Chief Investigator (CI) [CI's CV]		01 August 2018
Summary CV for student [PI CV]		28 February 2018
Summary CV for supervisor (student research) [Heather Cassie's CV]		01 September 2018
Summary CV for supervisor (student research) [John Radford's CV]		01 September 2018

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document *"After ethical review – guidance for researchers"* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol

- Progress and safety reports
- Notifying the end of the study

The HRA website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website: http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/

HRA Learning

We are pleased to welcome researchers and research staff to our HRA Learning Events and online learning opportunities– see details at: https://www.hra.nhs.uk/planning-and-improving-research/learning/

19/ES/0042	**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project.

Yours sincerely

pp
Mrs Natalie McInally
Vice-chair

Email: eosres.tayside@nhs.net

Enclosures: "After ethical review – guidance for researchers"

Copy to: TASC

Appendix 13 The parents information sheets for the multi-methods study with parents and children

Parents Information Sheet (Interview and questionnaire)

Study Title: Parents/carers' and children's views of silver diamine fluoride for the management of carious lesions in children: a multi-methods study

Study Researcher*:* Nassar Seifo

Supervisors: Prof. Nicola Innes, Dr. John Radford and Dr. Heather Cassie

Sponsors: University of Dundee and NHS Tayside

What do you and your child think of a new way to treat children's decayed baby teeth?

We would like to invite you to take part in this research study

We are asking you to consider taking part in a research study about a new kind of fluoride that dentists can put on children's teeth to stop tooth decay after it has started. This forms part of a PhD project of Nassar Seifo within the School of Dentistry at the University of Dundee. We want to explore children's and parent/carers' views on this new fluoride; Silver Diamine Fluoride (SDF). The project is explained more in this leaflet.

Your responses to the questions will be made anonymised and kept confidential. Each interview will be assigned a number code to ensure there are no personal identifiers when we look at your responses or in reports about this study. Your participation will be a valuable to our research and may help to inform the future care of children with tooth decay.

Please take time to read the enclosed information sheet carefully and think about whether or not you would like to take part.

This study is sponsored by the University of Dundee and NHS Tayside. It is funded by the University of Dundee. The study is being organised by Professor Nicola Innes, Professor of paediatric dentistry.

Throughout this leaflet we call parents or the people who look after the child "parents" for simplicity.

What is the project's purpose?

This research project aims to explore what children and parents think of a new approach for treating decayed teeth in children. Tooth decay is caused by bacteria growing on the tooth's surface destroying the tooth surface and causing a cavity. The traditional treatment is injection, drilling and filling, or placing silver crowns on the teeth. However, there is a new approach that is less invasive. It involves applying a liquid; SDF onto the cavities to kill the bacteria, make the tooth stronger and stop the decay getting worse. Participating in this study does not mean that your child will receive any treatment. You and your child will only be asked what you think about this treatment by looking at some pictures and talking to us.

What will happen to me if I take part?

- If you are interested in taking part, you will kindly complete the attached reply slip, then you either bring it with you on your next visit to the Dundee Dental School and Hospital and put it in a box in the reception and the Child Dental Health clinic if your next scheduled visit is within two weeks, or post it using the freepost envelope attached.
- You will be contacted by a researcher and invited to attend an appointment at Dundee Dental School and Hospital with your child.
- We will tell you more about the study and you will be asked to sign a consent form if you agree to take part.
- We will show you and your child some images of decayed teeth before and after treatment and ask you some questions. These will focus on your child's previous dental experiences and about your thoughts of this new treatment approach, the interview will be audio recorded and is estimated to last between 20 and 60 minutes. There will be a short interview with you followed by a short discussion with your child. However, your child will be with you all the time.
- After the interview you will also be asked to fill out a questionnaire that takes around 10 mins to complete. The questionnaire is about this new SDF treatment and how likely you might be to choose it, if your child had decayed baby teeth in the future. The questionnaire contains pictures of decayed teeth before and after treatment using SDF along with several treatment approaches These picture will help you to see what the treatment looks like and help you to think about which treatment you would choose if your child had decay in their baby teeth and needed treatment.
  At the end of the questionnaire, there is a question for your child to answer, or you can complete it with your child if they are too young to complete it by themselves. The question asks how your child feels about going to the dentist to have their teeth checked. The questionnaire will not be linked to any clinical data. There is nothing else you have to do after that.

All participants in the questionnaire/interview part will receive a £10 Love2Shop voucher to thank them for taking part.

Why have I been chosen?

You have been chosen because this study is about children who are 4 to 12 years old and you are the parent/guardian of a child of this age. Around 20 parents and 20 children are expected to take part in the study.

Do I have to take part?

No. It is up to you to decide. Participation in this study is entirely voluntary and you are free to refuse to take part or to withdraw from the study at any time without having to give a reason and without this affecting your future medical care or your relationship with medical or nursing staff looking after you.

What will happen with the information collected about me?

Identifiable information about you and the information collected about you during the trial/study will be stored securely by the University of Dundee. Only specified members of the research team will have access to this information. Your identifiable information and your anonymised and coded study information will be stored securely on a password-protected database(s) in the University of Dundee.

Your information will be kept securely for five years after the end of the study. After five years all identifiable information will be removed and the anonymised information will be kept for research purposes. It will only be made available to trial team members/ investigators if a formal request describing their plans is approved by the School of Dentistry Research Ethics Committee.

What are the possible disadvantages and risks of taking part?

There are no known risks or disadvantages to you from taking part in the study. However, during the interview you and your child will be shown images of decayed teeth before treatment and after treatment using different ways of managing them. Some people may find these images unpleasant to look at. The questionnaire contains similar images of decayed teeth before and after treatment. There are also a few questions about dental treatment for children under general anaesthesia (while they are asleep) which can be stressful for some parents to think about.

You don't have to tell us anything you don't want to. If you feel upset during the interview, we will ask you if you wish to take a break or if you wish to stop the interview. If you agree, we will ask a member of the care team to support you.

What are the possible benefits of taking part?

Taking part in the study will help to tell us how best to care for children with decayed teeth in the future. It is hoped that this work will help find out more about whether this is a good treatment for decayed baby teeth to prevent pain and infection without needing to use fillings, crowns or injections.

What if something goes wrong?

If you have any concerns about your participation in the study, you have the right to raise your concern with a researcher involved in conducting the study or a doctor involved in your care.

If you have a complaint about your participation in the study, you should first talk to a researcher involved in the study. However, you have the right to raise a formal complaint. You can make a complaint to a senior member of the research team or to the Complaints Officer for NHS Tayside.

Complaints and Feedback Team, NHS Tayside, Ninewells Hospital, Dundee, DD1 9SY.
Freephone: 0800 027 5507
Email: feedback.tayside@nhs.net

In the event that you think you have suffered harm as a result of your participation in the/study there are no automatic financial compensation arrangements. However, you may have the right to make a claim for compensation. Where you wish to make a claim, you should consider seeking independent legal advice, but you may have to pay for your legal costs.

Insurance

The University of Dundee and Tayside Health Board are Co-Sponsoring the study. The University of Dundee maintains a policy of public liability insurance which provides legal liability cover in respect of damages, costs and expenses arising out of claims.

Tayside Health Board is a member of the NHS Scotland Clinical Negligence and Other Risks Insurance Scheme (CNORIS) which provides legal liability cover of NHS Tayside in relation to the study. As the study involves University of Dundee staff undertaking clinical research on NHS Tayside patients, such staff hold honorary contracts with Tayside Health Board which means they will have cover under Tayside's membership of the CNORIS scheme.

Who has reviewed this study?

The East of Scotland Research Ethics Service REC 1, which has responsibility for scrutinising all proposals for medical research on humans, has examined the proposal and has raised no objections from the point of view of research ethics. It is a requirement that your records in this research, together with any relevant medical records, be made available for scrutiny by monitors from University of Dundee and NHS Tayside whose role is to check that research is properly conducted and the interests of those taking part are adequately protected.

Contact details for further information.

Nassar Seifo (PhD Candidate and Researcher)
Tel: +44 (0)1382 381693
email: nseifo@dundee.ac.uk

Professor Nicola Innes (Professor of Paediatric Dentistry)
Tel: +44 (0)1382 381631
email: n.p.innes@dundee.ac.uk

Data Protection Privacy Notice

How will personal information be used?

We will only use your personal information to carry out this study. The University of Dundee and NHS Tayside are the sponsors for this study based in the United Kingdom. We will be using information from you five years after the study has finished.

Your rights to access, change or move your information are limited, as we need to manage your information in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained unless you ask us not to. To protect your rights, we will use the minimum amount of information which is personably identifiable as possible.

Lawful reason for using your information

It is lawful for the University/NHS Tayside to use your personal data to ask you if you would like to take part in this study. The legal reason for using your information is that using it is necessary for the research which is carried out in the public interest.

You can find out more about how we will use your information at http://www.ahspartnership.org.uk/tasc/for-the-public/how-we-use-your-information and https://www.dundee.ac.uk/information-governance/dataprotection/ and at http://www.nhstayside.scot.nhs.uk/YourRights/PROD_298457/index.htm

or by contacting Research Governance, Tayside Medical Science Centre (TASC), 01382 383900 email tascgovernance@dundee.ac.uk

If you wish to complain about the use of your information please email dataprotection@dundee.ac.uk or, informationgovernance.tayside@nhs.net or, you may wish to contact the Information Commissioner's Office.

Thanks for taking time to read this information and for considering participating in this study.

Participant Information Sheet (Questionnaire)

Study title: Parents/carers' and children's views of silver diamine fluoride for the management of carious lesions in children: a multi-methods study
Study researcher*:* Nassar Seifo
Supervisors: Prof. Nicola Innes, Dr. John Radford and Dr. Heather Cassie
Sponsors: University of Dundee and NHS Tayside

What do you and your child think of a new way to treat children's decayed baby teeth?

We would like to invite you to take part in this research study

We are asking you to consider taking part in a research study about a new kind of fluoride that dentists can put on children's teeth to stop tooth decay after it has started. This forms part of a PhD project of Nassar Seifo within the School of Dentistry at the University of Dundee. We want to explore children's and parent/carers' views on this new fluoride; Silver Diamine Fluoride (SDF). The project is explained more in this leaflet.

Your responses to the questions will be made anonymised and kept confidential. Your participation will be a valuable to our research and may help to inform the future care of children with tooth decay.

Please take time to read the enclosed information sheet carefully and think about whether or not you would like to take part.

This study is sponsored by the University of Dundee and NHS Tayside. It is funded by the University of Dundee. The study is being organised by Professor Nicola Innes, Professor of Paediatric Dentistry

What is the project's purpose?

This research project aims to explore what children and parents think of a new approach for treating decayed teeth in children. Tooth decay is caused by bacteria growing on the tooth's surface destroying the tooth surface and causing a cavity. The traditional treatment is injection, drilling and filling, or placing silver crowns on the teeth. However, there is a new approach that is less invasive. It involves applying a liquid; SDF onto the cavities to kill the bacteria, make the tooth stronger and stop the decay getting worse. Participating in this study does not mean that your child will receive any treatment. You and your child will only complete a questionnaire about what you think of your child's previous visits to the dentist and to prioritise few treatments options.

What will happen to me if I take part?

You will complete the attached questionnaire. The questionnaire is about this new SDF treatment and how likely you might be to choose it, if your child had decayed baby teeth in the future. The questionnaire contains pictures of decayed teeth before and after treatment using SDF along with several treatment approaches These picture will help you to see what the treatment looks like and help you to think about which treatment you would choose if your child had decay in their baby teeth and needed treatment.

At the end of the questionnaire, there is a question for your child to answer, or you can complete it with your child if they are too young to complete it by themselves. The question asks how your child feels about going to the dentist to have their teeth checked. The questionnaire will not be linked to any clinical data.

You can return it either by post using freepost envelope provided with this leaflet or you can bring it with you to the clinic if your child has an upcoming appointment at the clinic soon. There is a box for it on the clinic. Returning of the completed questionnaire will be an implied consent to take part in the study.

Why have I been chosen?

You have been chosen because this study is about children who are 4 to 12 years old and you are the parent of a child of this age. It is anticipated that around 120 parents with their children will take part in the study.

Do I have to take part?

No. It is up to you to decide. Participation in this study is entirely voluntary and you are free to refuse to take part or to withdraw from the study at any time without having to give a reason and without this affecting your future medical care or your relationship with medical or nursing staff looking after you.

What will happen with the information collected about me?

The information collected about you during the study will be stored securely by the University of Dundee. Only specified members of the research team will have access to this information. Your identifiable information and your anonymised and coded study information will be stored securely on a password-protected database in the University of Dundee.

Your information will be kept securely for five years after the end of the study. After five years all identifiable information will be removed and the anonymised information will be kept for research purposes. It will only be made available to trial team members/ investigators if a formal request describing their plans is approved by the School of Dentistry Research Ethics Committee.

What are the possible disadvantages and risks of taking part?

There are no known risks or disadvantages to you from taking part in the study. However, the questionnaire contains images of decayed teeth before treatment and after treatment using different ways of managing them. Some people may find these images unpleasant to look at

There are also a few questions about dental treatment for children under general anaesthesia (while they are asleep) which can be stressful for some parents to think about. You don't have to tell us anything you don't want to.

What are the possible benefits of taking part?

Taking part in the study will help to tell us how best to care for children with decayed teeth in the future. It is hoped that this work will help find out more about whether this is a good treatment for decayed baby teeth to prevent pain and infection without needing to use fillings, crowns or injections.

What if something goes wrong?

If you have any concerns about your participation in the study, you have the right to raise your concern with a researcher involved in conducting the study or a doctor involved in your care.
If you have a complaint about your participation in the study, you should first talk to a researcher involved in the study. However, you have the right to raise a formal complaint. You can make a complaint to a senior member of the research team or to the Complaints Officer for NHS Tayside.

Complaints and Feedback Team, NHS Tayside, Ninewells Hospital, Dundee, DD1 9SY.
Freephone: 0800 027 5507
Email: feedback.tayside@nhs.net

In the event that you think you have suffered harm as a result of your participation in the/study there are no automatic financial compensation arrangements. However, you may have the right to make a claim for compensation. Where you wish to make a claim, you should consider seeking independent legal advice, but you may have to pay for your legal costs.

Insurance

The University of Dundee and Tayside Health Board are Co-Sponsoring the study. The University of Dundee maintains a policy of public liability insurance which provides legal liability cover in respect of damages, costs and expenses arising out of claims.
Tayside Health Board is a member of the NHS Scotland Clinical Negligence and Other Risks Insurance Scheme (CNORIS) which provides legal liability cover of NHS Tayside in relation to the study. As the study involves University of Dundee staff undertaking clinical research on NHS Tayside patients, such staff hold honorary contracts with Tayside Health Board which means they will have cover under Tayside's membership of the CNORIS scheme.

Who has reviewed this study?

The East of Scotland Research Ethics Service REC 1, which has responsibility for scrutinising all proposals for medical research on humans, has examined the proposal and has raised no objections from the point of view of research ethics. It is a requirement that your records in this research, together with any relevant medical records, be made available for scrutiny by monitors from University of Dundee and NHS Tayside whose role is to check that research is properly conducted and the interests of those taking part are adequately protected.

Contact details for further information.

Nassar Seifo (PhD Candidate and Researcher)
Tel: +44 (0)739 7723 222
email: nseifo@dundee.ac.uk

Professor Nicola Innes (Professor of Paediatric Dentistry)
Tel: +44 (0)1382 381631
email: n.p.innes@dundee.ac.uk

Data Protection Privacy Notice

How will personal information be used?

We will only use your personal information to carry out this study. The University of Dundee and NHS Tayside are the sponsors for this study based in the United Kingdom. We will be using information from you five years after the study has finished.

Your rights to access, change or move your information are limited, as we need to manage your information in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained unless you ask us not to. To protect your rights, we will use the minimum amount of information which is personably identifiable as possible.

Lawful reason for using your information

It is lawful for the University/NHS Tayside to use your personal data to ask you if you would like to take part in this study. The legal reason for using your information is that using it is necessary for the research which is carried out in the public interest.

You can find out more about how we will use your information at http://www.ahspartnership.org.uk/tasc/for-the-public/how-we-use-your-information and https://www.dundee.ac.uk/information-governance/dataprotection/ and at http://www.nhstayside.scot.nhs.uk/YourRights/PROD_298457/index.htm

or by contacting Research Governance, Tayside Medical Science Centre (TASC), 01382 383900 email tascgovernance@dundee.ac.uk

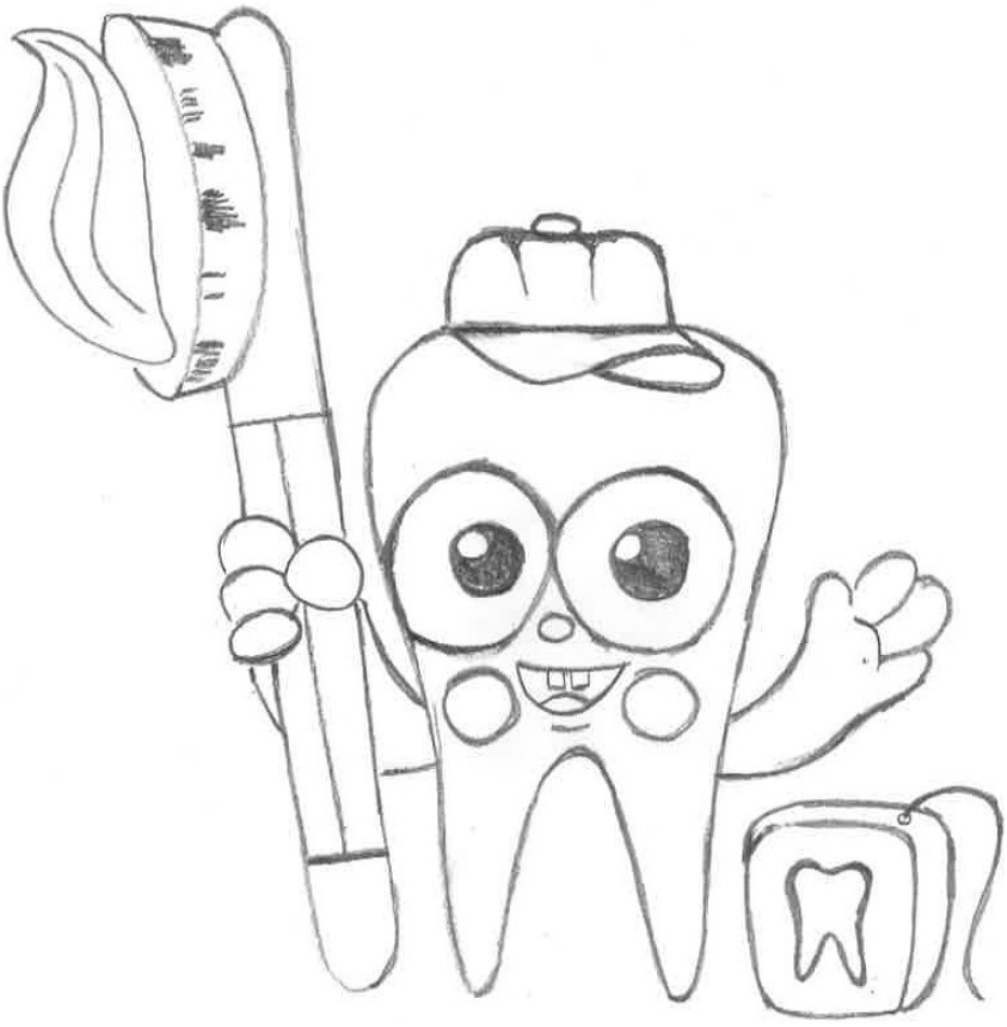
If you wish to complain about the use of your information please email dataprotection@dundee.ac.uk or, informationgovernance.tayside@nhs.net or, you may wish to contact the Information Commissioner's Office.

Thanks for taking time to read this information and for considering participating in this study.

Appendix 14 The children information sheets for the multi-methods study with parents and children

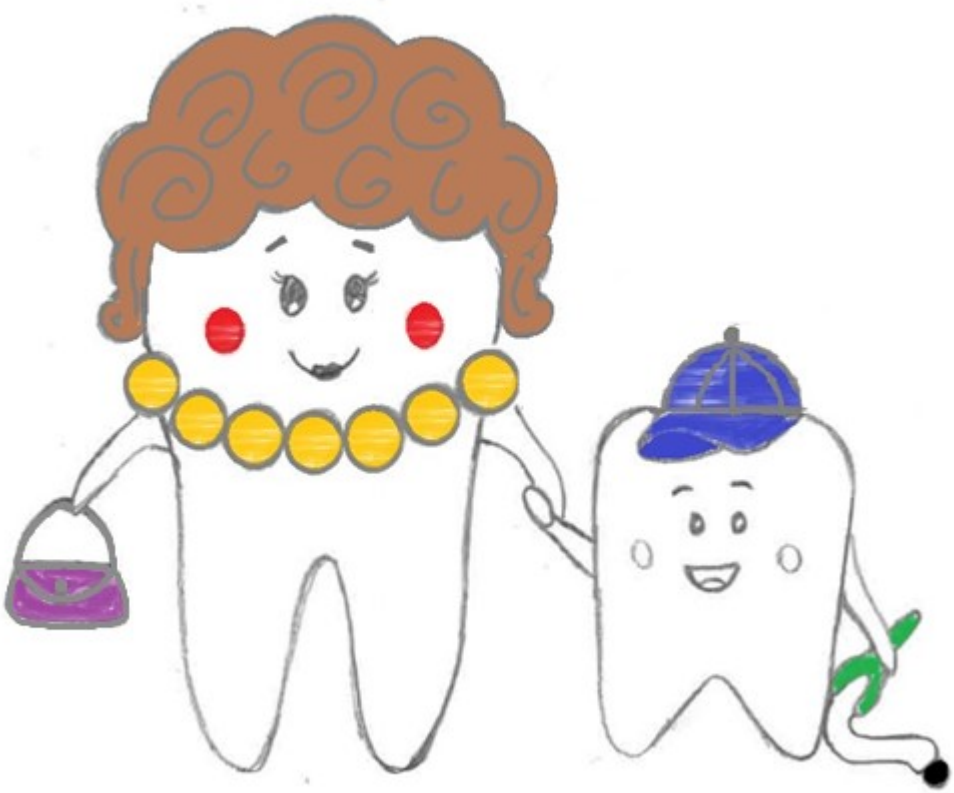
Children information sheet (preschool children)

Toothy's adventure with the dentist



Hi, I am toothy. Can you colour me in.

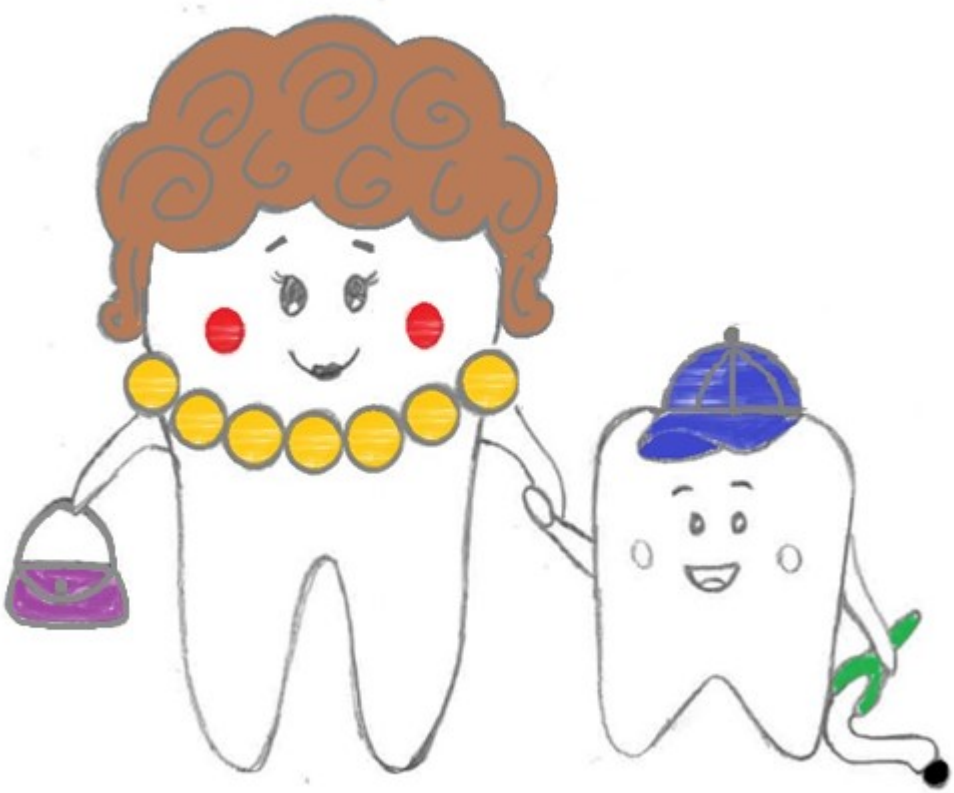
I'm here to help the dentist.



I am going to see the dentist today with the person looking after me.

We are talking to the dentist about teeth.

Can you tell us what you think?



All done. Time to go home.

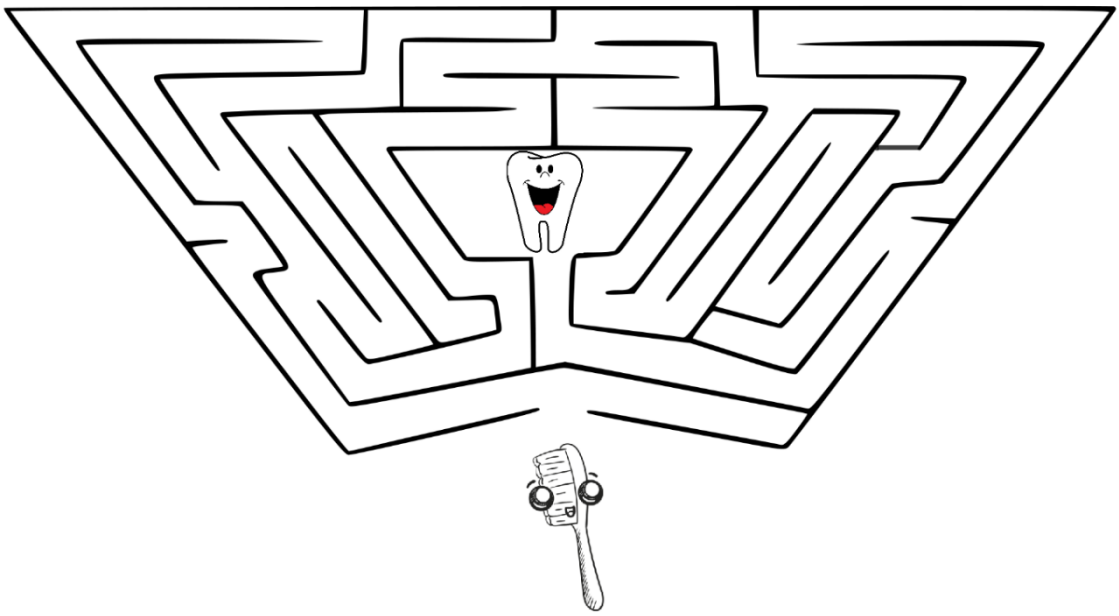
it was lots of fun.

Remember to bring me along to your visit.

Thank you.

Children information sheet (P1-P3)

What do you think of a new way to treat children's decayed baby teeth?



Help the toothbrush to get to the tooth.

Hello, my name is Nassar, I am working with dentists to find out what you think of a new way to look after children's teeth. Would you help me?

Why are you asking me?

You are the right age and come to Dundee Dental Hospital.

Do I have to take part?

No, you don't have to take part, and nobody will mind.

What will I have to do?

You and the person who looks after you, will come to Dundee Dental Hospital to tell us what you think about a new way to look after teeth

Can I stop at any time?

Yes, you can. We won't mind.

What should I do next?

Talk to the person who looks after you. You can both decide if you are going to take part.

Thank you for reading this.

Children information sheet (P4-P7)

Participant Identification Number:

What do you think of a new way to treat children's decayed baby teeth?

Hello, my name is Nassar, I am working with dentists to find out what children and the people that look after them think of a new way to look after children's teeth. Will you help me?

Before you decide, you need to know what the research study is about. Please read this leaflet and you can also ask someone to help you. If something doesn't make sense, or you have questions, you or your parent can ask us and we can discuss it.

What is research? Why this research is being done?

Research is one way to try to answer questions.
The question we want to answer is: What do parents and children think of a new way to treat children's teeth?

Why have I been asked to take part?

You have been asked to take part because you are the right age and you come to Dundee Dental Hospital.

Do I have to take part?

No, you don't. It is your choice whether you want to take part and you can always change your mind.

Did anyone else check the study is OK to do?

Before any research can go ahead, it has to be checked by a group of people to make sure that the research is fair.

What will happen to me if I take part?

Once we have checked that you and your parent, are happy for you to take part, we will invite you both to Dundee Dental Hospital, then you and your parent can ask any questions you have, then we will ask you and your parent some questions.

Will taking part help me?

It may not help you, but it will help other children.

What happens when the research study ends?

The research will be talked about and written down, but no one will know that you took part. All your information will be kept private.

What do I do if I don't want to take part in the research anymore?

Just tell your parent you that you don't want to take part anymore. You don't have to give any reason. It is your choice.

FIND AND CIRCLE THE WORDS IN THE PUZZLE

Toothbrush	Tongue
Dentist	Care
Child	Teeth
Smile	Dental
Floss	Brush
Gums	Mouth
Cavity	

S	C	A	D	E	N	T	I	S	T
M	A	C	A	V	I	T	Y	D	O
U	R	F	R	O	F	O	I	E	O
G	E	N	H	C	L	B	F	N	T
H	T	E	E	T	O	H	B	T	H
E	C	K	U	D	S	A	L	A	B
T	L	M	L	U	S	T	M	L	R
S	B	I	R	M	B	G	B	S	U
D	H	B	M	O	U	T	H	F	S
C	A	D	H	S	E	R	N	O	H

Thank you for reading this.

Appendix 15 The reply slip for the multi-methods study with parents and children

Reply slip

Study title: Parents/carers' and children's views of silver diamine fluoride for the management of carious lesions in children: a multi-methods study

Principal Investigator: Nassar Seifo

Chief Investigator: Professor Nicola Innes

For more information or to take part in the study, please contact Nassar Seifo in the research team by telephone, email or post.

☎ Tel 01382381693

Email nseifo@dundee.ac.uk

Post **Please complete the form below and place it in box at the receptionist's desk in the Children's Department at Dundee Dental Hospital and School, or send it by post using the freepost envelope provided.**

✂ ----------

Yes, I would like to find out more about this study. Please contact me.

My Name

……

…

My child is _____ year-old Boy / Girl (please circle)

My contact details:	Best way to contact me (please tick):	Best time to call:
Day time number: ……	☐	……
Mobile number: ……	☐	……
Email address: ……	☐	……

If you would like to contact the research team instead of posting the reply slip, please find our contact details on the information sheet about the study.

Appendix 16 The informed consent form for the multi-methods study with parents and children

University of Dundee

NHS Tayside

INFORMED CONSENT FORM

Participant Identification Number:

Study Title: Parents/Carers' and children's views of silver diamine fluoride for the management of carious lesions in children: a multi-methods study

Study Researcher: Nassar Seifo

Sponsors: University of Dundee and NHS Tayside

Please put initials in the box if you agree with the statement

1. I confirm that I have read the information sheet (dated .....version.....) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
2. I understand that my/my child's participation is voluntary and that my child and I are free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. ☐
3. Any data collected up to the point of withdrawal from the research will be kept anonymously and used for research purposes. This will include research publications. ☐
4. I agree that anonymised information about I and my child may be shared outside our clinical care team (or the research team) where it is needed to carry out for this study. ☐
5. I agree that anonymised information about my child and I collected for this study may be used in ethically approved medical research in the future. Any information which identifies my child and I will be removed before it is shared" for statements. ☐
6. I understand that personal data about my child and I, and research data collected during the study will be stored by the University of Dundee. ☐
7. I understand that relevant sections of my/my child's data collected during the study, may be looked at by the researchers and research team, the sponsors or regulatory authorities where it is relevant to my taking part in this research. I give permission for this. ☐
8. I understand that the data collected about my child and I by the researchers and research team in this study may be used to support other research in the future and may be shared anonymously with other researchers collaborating with the sponsors. ☐
9. I understand that the study involves a one-to-one interview, which includes my child and I. ☐
10. I understand that the interview will be audio recorded, anonymised and typed up. ☐
11. I agree to taking part in the above study. ☐
12. I agree to my child taking part in the above study ☐

----------	----------	----------
Name of parent/carer (CAPITALS)	Date	Signature
_____	_____	_____
Name of person taking consent (CAPITALS)	Date	Signature

1 for participant, 1 to be kept in medical records and 1 for study file.

Appendix 17 The child assent form for the multi-methods study with parents and children

University of Dundee

NHS Tayside

Child assent form

Participant Identification Number:

Study Title: Parents/Carers' and children's views of silver diamine fluoride for the management of carious lesions in children: a multi-methods study

Study Researcher: Nassar Seifo

Sponsors: University of Dundee and NHS Tayside

	Please put a circle round the one you agree with:
1. Has someone read you the information about this study?	Yes / No
2. Has somebody told you what this study is about?	Yes / No
3. Do you understand what this study is about?	Yes / No
4. Have you asked all the questions you want?	Yes / No
5. Have your questions been answered OK?	Yes / No
6. Do you understand it's OK to stop taking part at any time?	Yes / No
7. Are you happy to take part?	Yes / No

If any answers are 'no' or you don't want to take part, don't write your name!

If you do want to take part, you can write your name below.

_____	_____	_____
Name of child (please PRINT name)	Date	Child to write name here
_____	_____	_____
Name of person taking consent	Date	Signature

1 for participant, 1 to be kept in medical records and 1 for study file.

Appendix 18 The questionnaire for the multi-methods study with parents and children

University of Dundee

NHS Tayside

Parents/children Questionnaire

Study Title: Parents/carers' and children's views of silver diamine fluoride for the management of carious lesions in children: a multi-methods study
Study Researcher: Nassar Seifo
Sponsors: University of Dundee and NHS Tayside

If you have more than one child, please answer the questionnaire with only one of your children in mind. The questionnaire is about baby teeth and how they might be treated. There are no right or wrong answers.

Do you agree to complete the questionnaire? ☐ Yes ☐ No

1- Are you the parent or do you have parental responsibilities for the child? ☐ Yes ☐ No

2- Please identify your sex. ☐ Male ☐ Female ☐ Prefer not to say

3- How old is your child? _____ years-old

4- What class is your child in? ☐ Pre-school ☐ P1-P3 ☐ P4-P7

5- Please tick which your child is. ☐ Boy ☐ Girl

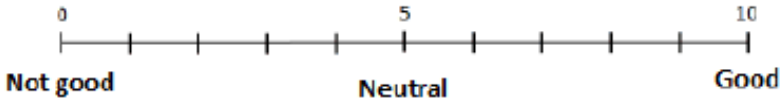
6- How often does your child brush their teeth or have their teeth brushed for them each day?
☐ Never ☐ Once ☐ Twice ☐ Three time or more

7- Has your child ever had a decayed tooth? ☐ Yes ☐ No

8- Has your child been to the dentist before today? ☐ Yes ☐ No

9- Has your child ever had a decayed tooth treated (filling or crown)? ☐ Yes ☐ No

10- How would you rate your child's overall experience at the dentist? (If applicable)



11- I think it is important to fix baby teeth.
☐ Strongly agree ☐ Agree ☐ Disagree ☐ Strongly disagree

12- I think it is important that my child's FRONT BABY TEETH look good after dental treatment.
☐ Strongly agree ☐ Agree ☐ Disagree ☐ Strongly disagree

13- I think it is important that my child's BACK BABY TEETH look good after dental treatment.
☐ Strongly agree ☐ Agree ☐ Disagree ☐ Strongly disagree

University of Dundee

NHS Tayside

Cavities (tooth decay) are caused by germs that produce acid that breaks down the teeth. We have a new way to treat cavities without injections. We can paint a liquid, called silver diamine fluoride or SDF for short, on the cavity that stops it from getting bigger. However, the liquid changes the colour of the cavity making it darker. The darker colour tells us that the treatment is effective. We are going to show you some pictures of cavities before and after this new treatment. We would like to know what you think of this treatment.

Back teeth before treatment

Back teeth after SDF treatment

14- If my child had cavities on their **BACK BABY TEETH**, I would find the discolouration from the new treatment (SDF) to be acceptable.

☐ Strongly agree ☐ Agree ☐ Disagree ☐ Strongly disagree

Front teeth before treatment

Front teeth after SDF treatment

15- If my child had cavities on their **FRONT BABY TEETH**, I would find the discolouration from the new treatment (SDF) to be acceptable.

☐ Strongly agree ☐ Agree ☐ Disagree ☐ Strongly disagree

University of Dundee

NHS Tayside

After looking at cavities following SDF treatment in the previous sheet, and the below photos of a crown and fillings, please answer the following questions.

Filling on a back tooth

Crown on a back tooth

Fillings on front teeth

16- If my child was fine (cooperative) to have fillings or crowns on their **back teeth**, I would choose SDF instead.
☐ Strongly agree ☐ Agree ☐ Disagree ☐ Strongly disagree

17- If my child was fine to have fillings on their **front teeth**, I would choose SDF instead.
☐ Strongly agree ☐ Agree ☐ Disagree ☐ Strongly disagree

18- If my child was upset but could cooperate enough to have fillings or crowns on their **back teeth**, I would choose SDF.
☐ Strongly agree ☐ Agree ☐ Disagree ☐ Strongly disagree

19- If my child was upset but could cooperate enough to have fillings on their **front teeth**, I would choose SDF instead.
☐ Strongly agree ☐ Agree ☐ Disagree ☐ Strongly disagree

20- If your child cried but could cooperate enough to have fillings or crowns on their **back teeth**, I would choose SDF instead.
☐ Strongly agree ☐ Agree ☐ Disagree ☐ Strongly disagree

21- If my child cried but could cooperate enough to have fillings on their **front teeth**, I would choose SDF instead.
☐ Strongly agree ☐ Agree ☐ Disagree ☐ Strongly disagree

22- If my child kicked/screamed and could not have fillings or crowns on their **back teeth**, I would choose SDF instead of trying to do fillings or crowns.
☐ Strongly agree ☐ Agree ☐ Disagree ☐ Strongly disagree

23- If my child kicked/screamed and could not have fillings on their **front teeth**, I would choose SDF instead of trying to do fillings.
☐ Strongly agree ☐ Agree ☐ Disagree ☐ Strongly disagree

24- If my child required general anaesthesia (put to sleep in the hospital) to take out their **back teeth**, I would choose SDF if it avoided them having to have their teeth taken out.
☐ Strongly agree ☐ Agree ☐ Disagree ☐ Strongly disagree

25- If my child required general anaesthesia (put to sleep in the hospital) to take out their **front teeth**, I would choose SDF if it avoided them having to have their teeth taken out.
☐ Strongly agree ☐ Agree ☐ Disagree ☐ Strongly disagree

University of Dundee

NHS Tayside

26- There are several things that may be important to you when deciding how your child's baby teeth are treated. We have listed some of them here (you can add other things that are important to you that are not included in the list).

Please prioritise these things by numbering them in order in the boxes, where 1 is for the most important thing to you, and 7 or 8 is the least important thing.

- ☐ Appearance of teeth after treatment
- ☐ Not receiving an injection
- ☐ One visit with no follow up visits
- ☐ No drilling
- ☐ Short appointment
- ☐ Success rate
- ☐ Short waiting time before treatment
- ☐ The treatment my child would prefer
- ☐ Others (please specify) .....

Please complete the next part with your child

Please ask your child to

"Point to the face that shows how you feel when you go to the dentist to have your teeth checked."

Thank you for completing this questionnaire

Appendix 19 The topic guide for the multi-methods study with parents and children

Topic Guide

Study title: Parents/Carers' and children's views of silver diamine fluoride for the management of carious lesions in children: a multi-methods study

Parents/carers interviews

Introduction

My name is Nassar Seifo, I am a trained Paediatric Dentist and doing a PhD at Dundee Dental School and Hospital. Thank you for coming and agreeing to participate in this study.

This study will basically explore what parent and children think of a type of fluoride. This fluoride agent that can actually stop the decay after it has started, but it stains the decayed bit of the tooth black permanently.

Can you go through the consent form and tick the boxes if you agree please?
Can we go through the assent form with your child?
Do you have any questions before we start?
Are you ok with me turning on the audio recorder now?

Let's move on the to the first part of this interview which will be about your child previous **DENTAL EXPERIENCE**

- Has your child been to the dentist before? If yes, what for?
- What did the dentist do?
- How often do you take your child to the dentist?
- How does your child feel about going to the dentist?
- Does anything concern you? if yes, what concerned you the most when your child was in the dental chair and why? If no, why?
- How was the overall experience at the dentist? Why?
- Has your child had any complications after the treatment? If yes, what?
- How would you feel about taking your child to the dentist again for similar treatment?

Moving on to the second part which explore your thoughts on **SILVER DIAMINE FLUORIDE**

- Here are photos of decayed teeth, what do think of them?
- Here are the same teeth after the dentist applied a liquid that stains the teeth but stops the decay, what do you think of them?
- How would you feel if your child received a treatment that would stain the tooth but prevent any pain or infection in the future, without local anaesthetic?
- Imagine that your child had a decayed in a milk tooth that will cause pain if left untreated. If the tooth was a back one, which of the following treatments you will choose? Why? (present photos of different treatments)
- What if the tooth was a front one, would it change your choice? why?
- If your child could not cope with treatment and the only option was to do treatment under inhaling (laughing) gas or avoid the inhalation gas by applying SDF, which option would you choose? Why?
- If your child could not cope with treatment and the only option was to extract the tooth with your child under general anaesthetic at hospital or avoid your child having a general anaesthetic by applying SDF, which option would you choose? Why?
- If you decided to choose SDF treatment, how do you feel about the need for this SDF to be re-applied every 6 months at the dentist?

Children interviews

- Can you remember going to the dentist?
- Can you remember why you went there?
- What did the dentist do?
- How did you feel there?
- Would it bother you to have your front/back tooth like this one (present SDF cases), why?